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Novel synthesis of 3-pyrrole substituted β-lactams via microwave-induced bismuth nitrate-catalyzed reaction

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ABSTRACT

Highly stereoselective synthesis of 3-pyrrole substituted β-lactams is accomplished. The first step involves the synthesis of 3-phthalimido substituted β-lactams following Staudinger cycloaddition reaction of acid chloride equivalent with imines. Synthesis of 3-amino β-lactams is achieved via the deprotection of phthalimido group with ethylenediamine. These 3-amino β-lactams are converted to a new series of *N*-substituted pyrroles at room temperature as well as using microwave-induced bismuth nitrate-catalyzed reaction with an excellent yield. Exclusive formation of *trans* pyrrole-substituted β-lactams is observed with *N*-chrysenyl system. The method is equally efficient for the synthesis of racemic as well as optically pure 3-pyrrole substituted β-lactams.

1. Introduction

Synthesis of β-lactams as biologically active compounds is very crucial. The use of β-lactams as antibiotics is experimentally proved by several thousands of papers and patents.[1] In contrast, we[2] and others[3] have reported limited research on anticancer β-lactams till now. The most important method for the preparation β-lactams is Staudinger cycloaddition reaction.[4] This reaction requires an imine, a tertiary base, and acid chloride (or equivalent). It is known that the stereochemistry of β-lactams varies depending on the substituents present in the imine, and acid chloride, and the conditions of the reactions. In contrast to the existing literature, we have disclosed that the reaction of polyaromatic imines with acid chloride in the presence of triethylamine produced *trans*-β-lactams. We describe herein stereocontrolled synthesis of a few novel 3-pyrrole substituted β-lactams (both racemic and optically pure). Some of these β-lactams have a chrysenyl group at the nitrogen-1 of the four-membered lactam ring.

In our earlier studies on anticancer drug development program, we have discovered[5] that the basicity of the compounds plays an important role in the determining their potency against a number of cancer cell lines. Our concept on the synthesis of 3-pyrrole-substituted β-lactams is further strengthened because pyrroles are found to be the fundamental structural motifs in various classes of natural and biologically important molecules,[6] such as porphyrins, bile pigments, coenzymes, and alkaloids. This moiety is also present[7] in several synthetic pharmaceuticals as well as electrically conducting polymers. However, despite huge applications, synthesis of 3-pyrrole substituted β-lactams is not explored systematically. Very recently, Tidwell et al. has described[8] a fascinating synthetic method of 3-pyrrole substituted β-lactams through Staudinger cycloaddition reaction. We present herein an expeditious synthetic method of 3-pyrrole-substituted β-lactams using bismuth nitrate pentahydrate-catalyzed modified Paal–Knorr reaction under microwave irradiation in the absence of any solvent. Optically active 3-pyrrole substituted β-lactams have also been successfully prepared using this newly developed method.

2. Results and discussion

During the course of investigation on pyrroles, we envision that 3-prrole substituted β-lactams can be easily synthesized if we use 3-amino β-lactams and 2,5-dimethoxytetrahydrofuran as the staring materials and react them in the presence of an acidic catalyst following Clauson–Kass (modified Paal–Knorr) method. The 3-amino β-lactams could be easily derived from 3-phtalimido β-lactams, which could be made through Staudinger cycloaddition reaction of imines and acid chloride (equivalent). On this basis, the retro-synthetic approach is described as follows.

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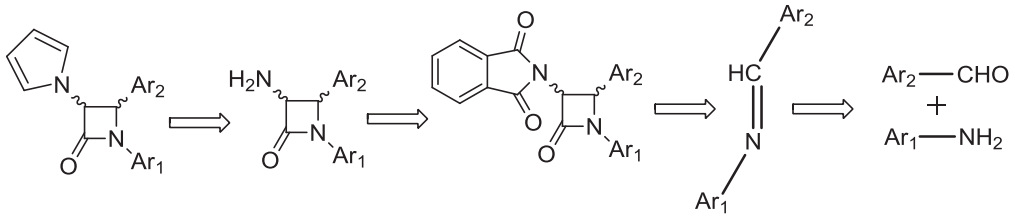


2.1. Synthesis of 3-phthalimido β-lactams

At the beginning of the approach, cycloaddition of imine with phthalimidoacetic acid (acid chloride equivalent) in presence of triethylamine was performed (Scheme 1).

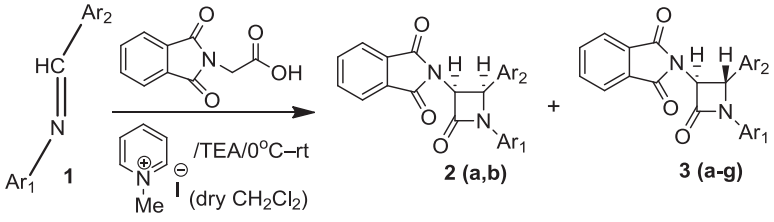
Reaction of *N*-phenyl and *p*-methoxyphenyl **1** with phthalimidoacetic acid in the presence of triethylamine and *N*-methylpyridinium iodide was performed at 0 °*C*-room temperature and a mixture of (±)-*cis* and (±)-*trans* β-lactams was isolated. However, polyaromatic imine **1** derived from 6-chrysenyl amine produced exclusively (±)-*trans* β-lactam. High temperature reaction also gave an identical result in comparable yield. The reaction proceeded well with diverse imines that have different types of aromatic groups (Scheme 1) in good to excellent yield of the products. The formation of mixture of isomeric products **2a**, **3a**, and **2b**, **3b** with their corresponding imines had cast doubt about the analysis of the product distributions of earlier studies. For example, while our current studies confirmed the formation of two isomeric *cis* and *trans* products, previous studies on the same reaction reported[1e–g] the formation of *trans* isomer only with imines that have monocyclic aromatic groups at the *C*- and *N*-terminus. The formation of *cis* isomer was observed with activated phthalimidoacetic acid and *N*-alkyl imine. Conjugated imine also produced the *cis* isomer. It appears that the electron withdrawing aromatic groups at the *C*- and N-terminus of the imine is responsible for the formation of the *trans* isomer. The effect of electron withdrawing properties is highly significant when chrysene group is present at the *N*-terminus of the imine. The formation of *trans* isomer in case of *N*-chrysenyl imines and *N*-diaryl imines can be rationalized through an isomerization of the enolate as described[2b,c] earlier. Polyaromatic group (in this example, chrysene) at the nitrogen stabilizes the iminium ion greatly. The electron withdrawal properties of monocyclic aromatic groups at the *N*-site of the imine are not sufficient to have a complete isomerization of the enolate and therefore, a mixture of *cis*- and *trans*-isomers is formed.

2.2. Preparation of 3-amino β-lactams

Having an attractive route for the synthesis of phthalimido-substituted β-lactams of diverse structures, our attention was turned to deprotect the phthalimido group. Deprotection of phthalimido group was investigated with hydrazine hydrate. However, the yields of the products were not satisfactory. In contrast, reaction of 3-phthalimido β-lactams with ethylenediamine at room temperature produced the corresponding 3-amino β-lactams in good yield. The stereochemistry of β-lactams remains unchanged during this conversation. No cleavage of the β-lactam rings was observed under this condition (Scheme 2).

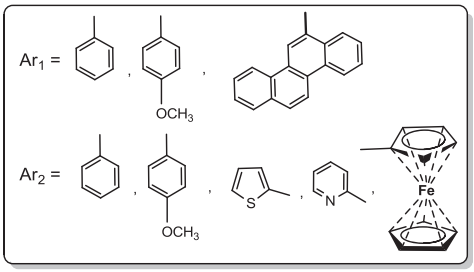
2.3. Preparation of 3-pyrrole-substituted β-lactams under microwave irradiation in the absence of solvents

We have been engaged in the microwave-induced reactions for many years. Using microwave irradiation technique we have successfully developed several new organic methodologies, which include stereoselective synthesis of β-lactams,[9] synthesis of pyrroles,[10] aza-Michael addition,[11] and synthesis of quinoxalines.[12] Parallel to this study, we have demonstrated the catalytic activity of trivalent bismuth nitrate pentahydrate in a number of reactions. These experiments have resulted in various methods that include nitration of aromatic systems,[13] Michael reaction,[14] protection of carbonyl compounds,[15] deprotection of oximes, and hydrazones,[16]

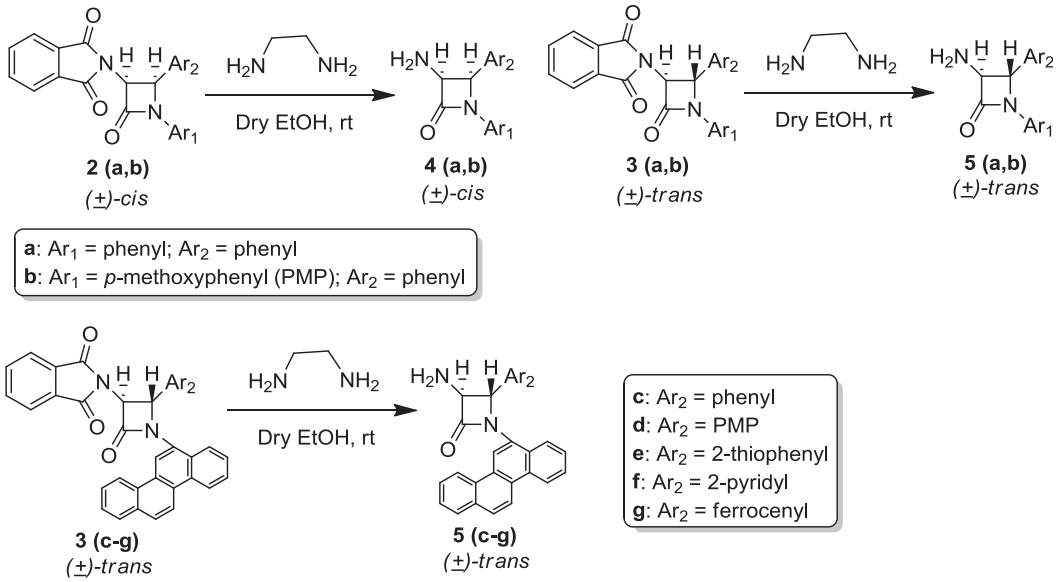


Ar_1 = phenyl, *p*-methoxyphenyl (PMP): *mixture of (±)-cis and (±)-trans isomers*
Ar_1 = 6-chrysenyl: *(±)-trans isomers*

a: Ar_1 = phenyl; Ar_2 = phenyl
b: Ar_1 = *p*-methoxyphenyl (PMP); Ar_2 = phenyl
c: Ar_1 = 6-chrysenyl; Ar_2 = phenyl
d: Ar_1 = 6-chrysenyl; Ar_2 = PMP
e: Ar_1 = 6-chrysenyl; Ar_2 = 2-thiophenyl
f: Ar_1 = 6-chrysenyl; Ar_2 = 2-pyridyl
g: Ar_1 = 6-chrysenyl; Ar_2 = ferrocenyl



Scheme 1. Synthesis of 3-phthalimido substituted β-lactams.



Scheme 2. Synthesis of 3-amino substituted β-lactams.

Paal–Knorr synthesis of pyrroles,[17] hydrolysis of amide,[18] electrophilic substitution of indoles,[19] synthesis of α-aminophosphonates,[20] and Biginelli condensation.[21] During the course of studies on bismuth nitrate-catalyzed reactions and microwave-induced methods, it has been conceived that 3-pyrrole substituted β-lactams can be easily prepared if we react 3-amino β-lactams with 2,5-dimethoxytetrahydrofuran. Our success in the bismuth nitrate-induced reaction has revealed that this reagent acts as a Lewis acid. Moreover, it has been discovered that this reagent is compatible in the presence of chemically sensitive functional groups and rings (amino group and four-membered cyclic amide).

Because of their interesting biological properties various methods for the synthesis of substituted pyrroles are described in the literature. We have identified an expeditious synthetic method for the preparation of pyrroles fused with β-lactams by reacting 3-amino β-lactams with 2,5-dimethoxytetrahydrofuran in the presence of catalytic amounts (5 mol %) of bismuth nitrate at room temperature. It has also been discovered that the reaction gives products with extreme rapidity under microwave irradiation. The presence of small amounts of catalyst (5 mol %) is necessary for the success of the reaction. Our initial work started with screening of catalyst loading to obtain optimal reaction conditions for the synthesis of 3-pyrrole substituted β-lactams. First of all, a number of bismuth salts, e.g., bismuth chloride, bismuth triflate, bismuth subnitrate, bismuth bromide bismuth iodide, and bismuth nitrate pentahydrate have been screened using 1 mmol of (±)-*trans* 3-amino-1-(chrysen-6-yl)-4-phenylazetidin-2-one (**5c**) with 1.2 mmol of 2,5-dimethoxytetrahydrofuran as a model reaction under automated CEM microwave irradiation (300 Watts, 50 °C, 20–45 psi, 5 min). The results are shown in Table 1.

Bismuth nitrate pentahydrate was found to be the best catalyst under this condition (Entry 6, Table 1). Without using any catalyst (only microwave irradiation) 24% yield of the product was isolated in 5 min (Entry 7, Table 1). The same reaction was used to optimize the amount of the catalyst (Table 2). The results show that 5 mol % bismuth nitrate pentahydrate was required to complete the reaction within 5 min (Entry 6, Table 2). The reaction was then performed in various solvents as well as in neat condition under an identical microwave power using bismuth nitrate pentahydrate (5 mol %) as the catalyst to identify the best condition (Table 3).

Table 1
Microwave-assisted synthesis of 3-pyrrole substituted β-lactam from 1 mmol of (±)-*trans* 3-amino-1-(chrysen-6-yl)-4-phenylazetidin-2-one with 1.2 mmol of 2,5-dimethoxytetrahydrofuran using bismuth-salts as catalyst (10 mol %) under solventless condition (5 min): catalyst optimization

Entry	Bi-salt (10 mol %)	Yield (%)[a]
1	$BiCl_3$	61
2	$Bi(OTf)_3$	54
3	BiI_3	43
4	$Bi_5O(OH)_9(NO_3)_3$	31
5	$BiBr_3$	41
6	$Bi(NO_3)_3.5H_2O$	83
7	No catalyst	24

[a] Isolated yield.

Table 2
Microwave-assisted synthesis of 3-pyrrole substituted β-lactam from 1 mmol of (±)-*trans* 3-amino-1-(chrysen-6-yl)-4-phenylazetidin-2-one with 1.2 mmol of 2,5-dimethoxytetrahydrofuran using bismuth nitrate pentahydrate as catalyst under solventless condition (5 min): optimization of the amount of the catalyst

Entry	$Bi(NO_3)_3 \cdot 5H_2O$ (mol %)	Yield (%)[a]
1	30	57
2	25	51
3	20	62
4	15	68
5	10	83
6	5	89
7	2	56
8	1	37

[a] Isolated yield.

From these conditions, it was proved that bismuth nitrate pentahydrate is the best catalyst for this reaction (Entry 8, Table 3). Considering the above observations we carried out a series of reaction using 3-amino β-lactams (1 mmol) with 2,5-dimethoxytetrahydrofuran (1.2 mmol) in presence of bismuth nitrate pentahydrate (5 mol %) under microwave irradiation (Table 4).

Bismuth nitrate pentahydrate, a solid salt is commercially available from a number of companies, very economical, and much less toxic than other Lewis acids. It is very convenient to conduct the reaction with bismuth nitrate because of its stability in the presence of moisture and oxygen.

Table 3
Microwave-assisted synthesis of 3-pyrrole substituted β-lactam from 1 mmol of (±)-*trans* 3-amino-1-(chrysen-6-yl)-4-phenylazetidin-2-one with 1.2 mmol of 2,5-dimethoxytetrahydrofuran using bismuth nitrate pentahydrate as catalyst (5 mol %) for 5 min: solvent optimization

Entry	Solvent (1 mL)	Yield (%)[a]
1	Water	67
2	THF	76
3	Ethanol	65
4	Toluene	47
5	Methanol	69
6	Dichloromethane	53
7	DMSO	70
8	Neat	89

[a] Isolated yield.

Table 4
Bismuth nitrate-induced synthesis of 3-pyrrole substituted β-lactams from 3-amino substituted β-lactams under solventless condition

Entry	Substrate (3-amino β-lactam)	Product (3-pyrrole β-lactam)	Condition A stirring at room temperature		Condition B MWI (50 °C, 300 Watts)	
			Time (h)	Yield (%)[a]	Time (min)	Yield (%)[a]
1	**4a**	**6a**	12	64	2	93
2	**4b**	**6b**	12	67	2	88
3	**5a**	**7a**	12	62	2	96
4	**5b**	**7b**	12	72	2	95
5	**5c**	**7c**	24	43	5	89
6	**5d**	**7d**	24	46	5	91
7	**5e**	**7e**	24	59	5	88
8	**5f**	**7f**	24	52	5	90
9	**5g**	**7g**	24	55	5	89
10	**10a**	**11a**	12	70	5	92
11	**10b**	**11b**	12	77	5	94

[a] Isolated yield.

The 3-amino β-lactam, 2,5-dimethoxytetrahydrofuran and bismuth nitrate (catalytic amounts) were mixed and stirred at room temperature. Upon extraction of the reaction mixture 80–90% yield of the products were obtained. In another method, the mixture was irradiated in an automated CEM microwave oven at 50 °C for 5 min using a power level of 300 Watts and 20–45 psi pressure in the absence of solvent.[22,23] The reaction proceeded equally well irrespective of the nature of substituent present in the β-lactam ring without any change of stereochemistry. The *trans* stereochemistry of the compound (**7g**) was further confirmed by X-ray crystallographic analysis[24] (Fig. 1, for description, see Ref. 24). The bismuth

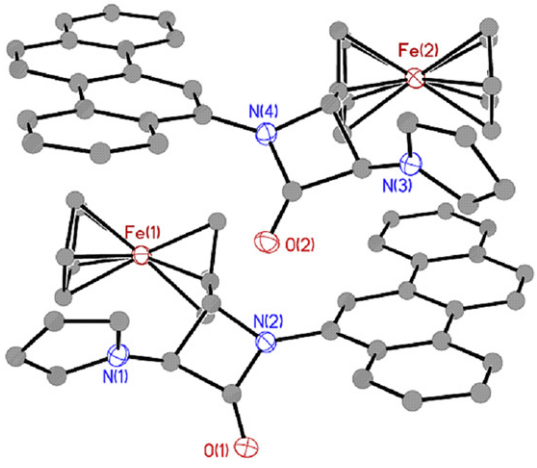
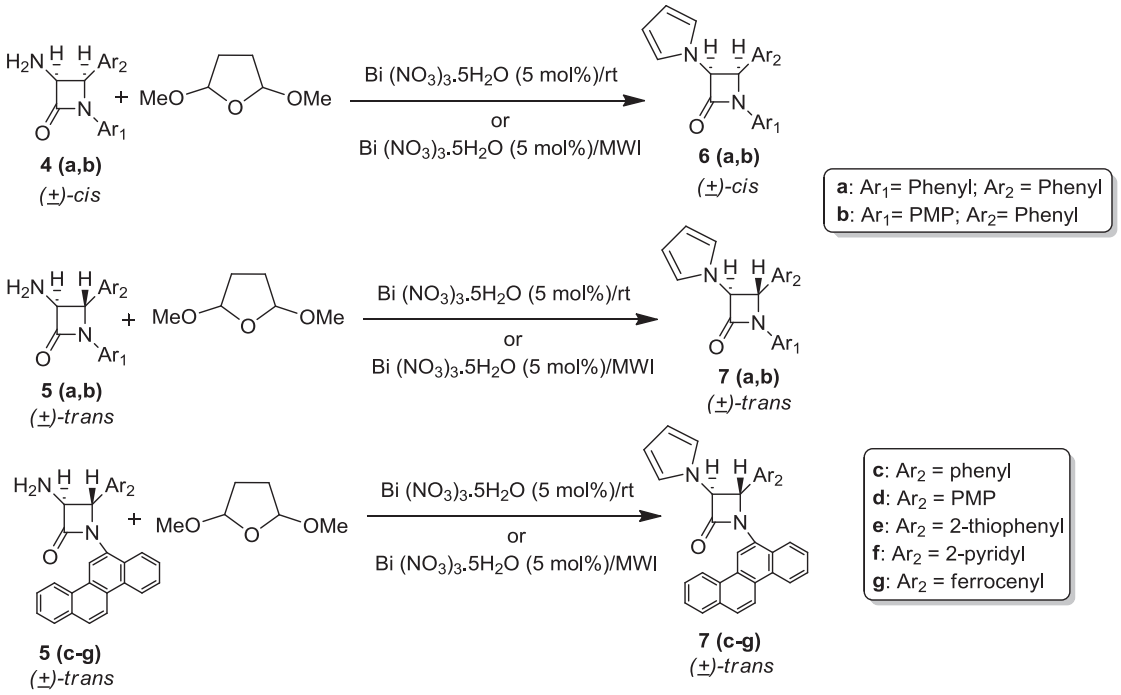


Fig. 1. X-ray crystallographic (ORTEP) structure of (**7g**).

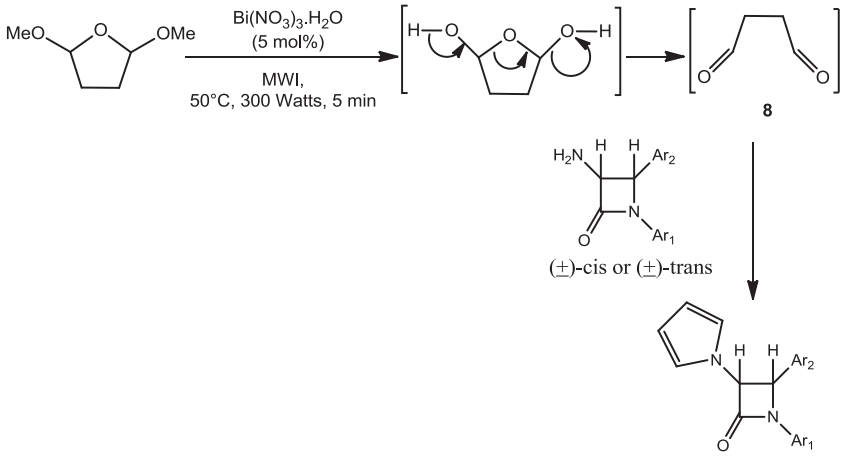
nitrate-catalyzed pyrrole formation reaction of 3-amino β-lactams as described herein is very simple and can be used with remarkable success.

A plausible mechanistic pathway for the synthesis of 3-pyrrole substituted β-lactams from 3-amino β-lactams is suggested (Scheme 4). The methoxy groups in 2,5-dimethoxytetrahydrofuran can undergo a deprotection reaction under mild acidic conditions and this process can be highly facilitated by microwave irradiation. The intermediate can easily form the reactive dialdehyde **8** (Scheme 4). The reactive dialdehyde **8** on reaction with 3-amino β-lactams can lead to the corresponding 3-pyrrole substituted β-lactams following a nucleophilic addition and subsequent dehydration-aromatization route. This reaction suggests the capability of bismuth nitrate to serve as a Lewis activator. ^{1}H NMR spectroscopy has been used to strengthen the proposed mechanism. Upon irradiating a $CDCl_3$ solution of 2,5-dimethoxytetrahydrofuran for 5 min, ^{1}H NMR has been taken. A downfield signal due to the −CHO group is observed. The intensity of the −CHO group becomes more predominant in the ^{1}H NMR when 2,5-dimethoxytetrahydrofuran was irradiated in $CDCl_3$ in the presence of catalytic amounts of bismuth nitrate. This suggests the formation of **8** in the reaction media in the presence of bismuth nitrate under microwave irradiation. Demethylation should take place in 2,5-dimethoxytetrahydrofuran because electrophilic reagent bismuth nitrate should attack 2,5-dimethoxytetrahydrofuran. The success of this reaction could be explained because of the release of nitric acid in the medium. However, reaction of a few substrates with catalytic amounts of nitric acid produced products with very low yields. Experiments were conducted with nitric acid that could be obtained from the decomposition of 5 mol % of bismuth nitrate pentahydrate. Two reactions described in Scheme 3 (**4a** and **4b**) were performed with 16.2 μL of concentrated nitric acid (24 mg of bismuth nitrate pentahydrate can liberate16.2 μL of concentrated nitric acid). However, results were disappointing since the yields of the products could not be increased. Low yields (10–20%) of the products were observed (not isolated). An increase of the amount of nitric acid was not helpful to increase the yield of the products. Although every attempt was made to use a precise amount of nitric acid and to obtain good yield of 3-pyrrole substituted β-lactams (10 mg–gram scale), however, the yields of the products could not be increased. Moreover, catalytic amounts of hydrochloric acid and sulfuric acid also failed to yield the desired products in satisfactory yields. In contrast, 3-pyrrole substituted β-lactams was prepared very easily in excellent yield with non-corrosive and crystalline bismuth nitrate pentahydrate. No special precaution was needed because bismuth nitrate is stable in the presence of air and moisture. The reaction was extremely fast. This method described herein can be classified under Paal–Knorr[25] or Clauson–Kass[26] reaction. Paal–Knorr prepared pyrroles by reacting a 1,4-dicarbonyl compound and an amine in the presence of acid/activator. Clauson–Kass synthesized pyrrole by reacting 2,4-deimethoxytetrahydrofuran and an amine in the presence of acid/activator. However, Clauson–Kass and our current study had confirmed that a reactive 1,4-dicarbonyl compound is really formed as an intermediate.

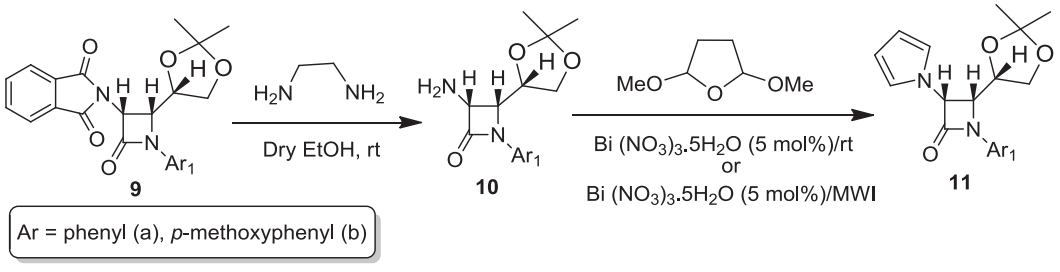
Finally, we have tested the efficacy of our procedure for the synthesis of optically active β-lactams. 3-Phthalimido substituted β-lactams (**9**) were synthesized from optically pure 2,2-dimethyl-1,3-dioxolane-4-carboxaldehyde following a published method from our laboratory.[27] The 3-phthalimido substituted β-lactams were deprotected by ethylenediamine as described above. The corresponding 3-amino substituted β-lactams (**10**) produced 3-pyrrole substituted β-lactams (**11**) upon treatment with 2,5-diemthoxytetrahydrofuran in the presence of catalytic amounts of bismuth nitrate pentahydrate at room temperature as well as under microwave-induced procedure (Scheme 5). Synthetic method for the preparation of optically active 3-pyrrole-substituted β-lactams,



Scheme 3. Synthesis of 3-pyrrole substituted β-lactams.



Scheme 4. Plausible mechanism for the synthesis of 3-pyrrole substituted β-lactams.



Scheme 5. Synthesis of 3-pyrrole substituted optically pure β-lactams.

following this strategy, is not known despite huge development in this area since 1945. Because of the mild conditions of the experiments, it is gratifying to note that no deprotection of the acid-sensitive ketal group to diol and subsequent oxidation, rearrangement, and lactonization was occurred in the synthesis of pyrroles (**11**) (Scheme 5).

3. Conclusions

In conclusion, a new synthetic strategy for the synthesis of novel 3-pyrrole substituted β-lactams in racemic and optically active forms is described. The procedure is equally effective with β-lactams that have different types of aromatic systems at the nitrogen and various substituents at C-4 of the ring. The extreme rapidity with excellent yield of the final step can be rationalized as a synergistic effect of the Lewis acid catalyst (bismuth nitrate) and microwave irradiation. In view of our earlier publications, this method may find future applications on anticancer therapeutics.

4. Experimental section

4.1. General

Melting points were determined in a Fisher Scientific electrochemical Mel-Temp* manual melting point apparatus (Model 1001) equipped with a 300 °C thermometer. FTIR spectra were registered on a Bruker IFS 55 Equinox FTIR spectrophotometer as KBr discs. ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) spectra were obtained at room temperature with Bruker superconducting Ultrashield™ Plus 600 MHz NMR spectrometer with central field 14.09 T, coil inductance 89.1 H, and magnetic energy 1127.2 kJ using $CDCl_3$ as solvent. Elemental analyses (C, H, N) were conducted using the Perkin–Elmer 2400 series II elemental analyzer, their results were found to be in good agreement (±0.2%) with the calculated values for C, H, N. Bismuth nitrate pentahydrate (reagent grade) 98% (Cat # 248592-500 G, Batch # MKBC6772) purchased from Sigma–Aldrich Corporation was used. All other chemicals were purchased from Sigma–Aldrich Corporation (analytical grade). Throughout the project solvents were purchased from Fisher–Scientific. Deionized water was used for the preparation of all aqueous solutions.

4.2. General procedure for the synthesis of 3-phthalimido β-lactam via the Staudinger reaction

A representative experimental procedure is described as follow. A solution consisting of phthalimidoacetic acid (*N*-phthaloylglycine) (1.5 mmol) in anhydrous dichloromethane (10 mL) was added 2-chloro-1-methylpyridinium iodide (Mukaiyama reagent, 3 mmol) and triethylamine (6 mmol) at ice-cold temperature. This mixture was stirred for 2 h. Imine (1 mmol) in dry dichloromethane (10 mL) was then added drop wise to this mixture at 0 °C. The reaction mixture was then stirred overnight at room temperature and monitored by TLC. After completion of the reaction, the reaction mixture was washed with saturated sodium bicarbonate solution (10 mL), brine (10 mL) and deionized water successively. The organic layer was dried with anhydrous sodium sulfate and evaporated to obtain the crude product. Column chromatography over silica gel was performed using ethyl acetate/hexanes mixtures to isolate the 3-phthalimido β-lactam in pure form. The *cis*:*trans* ratio was 2:1 for monoaromatic imines (Ar_1=phenyl, PMP; Scheme 1) but for *N*-chrysenyl imines *trans* isomers were obtained stereoselectively.

*4.2.1. (±)-cis-1,4-Diphenyl-2-oxo-4-phenylazetidin-3-yl isoindoline-1,3-dione (**2a**).* Yellow solid (61%); mp 181 °C; IR (KBr) 3012, 1759, 1716, 1623, 1503, 1104, 966, 748 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.79 (d, *J*=5.32 Hz, 1H), 5.53 (d, *J*=5.32 Hz, 1H), 7.07–7.85 (m, 14H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 59.90, 61.11, 117.35, 120.74, 123.44, 123.82, 127.17, 128.47, 129.12, 131.69, 134.24, 134.60, 137.11, 139.51, 161.95, 166.80. Anal. calcd for $C_{23}H_{16}N_2O_3$: C, 74.99; H, 4.38; N, 7.60. Found: C, 74.87; H, 4.31; N, 7.54.

*4.2.2. (±)-cis-1-(4-Methoxyphenyl)-2-oxo-4-phenylazetidin-3-yl isoindoline-1,3-dione (**2b**).* Yellow solid (64%); mp 157 °C; IR (KBr) 3255, 2905, 1759, 1720, 1511, 1452, 1299, 1116, 951, 718, 529 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.79 (s, 3H), 5.46 (d, *J*=5.58 Hz, 1H), 5.67 (d, *J*=5.52 Hz, 1H), 6.85–7.91 (m, 13H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.47, 58.94, 61.41, 114.16, 118.67, 123.73, 126.24, 128.39, 129.14, 131.02, 131.76, 134.21, 134.57, 156.89, 160.11, 166.85. Anal. calcd for $C_{24}H_{18}N_2O_4$: C, 72.35; H, 4.55; N, 7.03. Found: C, 72.31; H, 4.53; N, 6.94.

*4.2.3. (±)-trans-1,4-Diphenyl-2-oxo-4-phenylazetidin-3-yl isoindoline-1,3-dione (**3a**).* Reddish brown solid (33%); mp 200 °C; IR (KBr) 2955, 1763, 1712, 1599, 1385, 1084, 879, 711 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.28 (d, *J*=2.70 Hz, 1H), 5.39 (d, *J*=2.70 Hz, 1H), 7.11–7.92 (m, 14H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 61.23, 62.77, 117.63, 123.67, 124.50, 126.15, 129.14, 129.42, 131.85, 131.85, 134.45, 134.49, 135.83, 137.15, 162.04, 167.24. Anal. calcd for $C_{23}H_{16}N_2O_3$: C, 74.99; H, 4.38; N, 7.60. Found: C, 74.90; H, 4.28; N, 7.51.

*4.2.4. (±)-trans-1-(4-Methoxyphenyl)-2-oxo-4-phenylazetidin-3-yl isoindoline-1,3-dione (**3b**).* Brownish yellow solid (31%); mp 168 °C; IR (KBr) 3048, 2833, 1755, 1660, 1466, 1389, 1244, 1029, 826, 699 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.75 (s, 3H), 5.28 (d, *J*=2.59 Hz, 1H), 5.35 (d, *J*=2.58 Hz, 1H), 6.81–7.77 (m, 13H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.50, 60.90, 62.78, 114.41, 119.13, 123.82, 127.21, 128.47, 129.40, 131.19, 132.26, 134.34, 135.92, 156.54, 160.27, 166.93. Anal. calcd for $C_{24}H_{18}N_2O_4$: C, 72.35; H, 4.55; N, 7.03. Found: C, 72.27; H, 4.47; N, 6.98.

*4.2.5. (±)-trans-1-(Chrysen-6-yl)-2-oxo-4-phenylazetidin-3-yl isoindoline-1,3-dione (**3c**).* Yellow solid (76%); mp 272 °C; IR (KBr) 3246, 1765, 1716, 1597, 1451, 1388, 1095, 973, 753 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.60 (d, *J*=2.34 Hz, 1H), 5.89 (d, *J*=2.22 Hz, 1H), 7.27–7.94 (m, 17H), 8.49 (d, *J*=8.16 Hz, 1H), 8.63 (d, *J*=8.34 Hz, 1H), 8.71 (d, *J*=8.28 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 61.16, 62.72, 121.71, 122.59, 122.98, 123.91, 124.62, 126.71,126.96, 127.06, 127.25, 127.35, 127.85, 128.68, 129.15, 129.17, 129.81, 130.74, 131.10, 131.30, 131.82, 134.65, 135.65, 163.88, 167.07. Anal. calcd for $C_{35}H_{22}N_2O_3$: C, 81.07; H, 4.28; N, 5.40. Found: C, 81.00; H, 4.22; N, 5.32.

*4.2.6. (±)-trans-1-(Chrysen-6-yl)-2-(4-methoxyphenyl)-4-oxoazetidin-3-yl isoindoline-1,3-dione (**3d**).* Yellow solid (69%); mp 133 °C; IR (KBr) 3459, 2960, 2860, 2356, 1727, 1666, 1600, 1580, 1463, 1382, 1287, 1123, 1072, 1039, 957, 744 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.54 (s, 3H), 5.68 (d, *J*=2.46 Hz, 1H), 5.91 (d, *J*=2.28 Hz, 1H), 6.57 (d, *J*=9.12 Hz, 2H), 7.00 (d, *J*=8.52 Hz, 2H), 7.31–8.19 (m, 15H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.60, 68.16, 68.17, 105.94, 114.33, 114.65, 120.72, 120.79, 123.47, 123.69, 123.90, 126.66, 126.81, 128.09, 128.40, 128.59, 128.82, 128.90, 130.89, 131.86, 132.00, 132.47, 133.79, 133.95, 134.45, 134.63, 138.26, 139.55, 163.19, 167.76. Anal. calcd for $C_{36}H_{24}N_2O_4$: C, 78.82; H, 4.41; N, 5.11. Found: C, 78.75; H, 4.36; N, 5.02.

*4.2.7. (±)-trans-1-(Chrysen-6-yl)-2-oxo-4-(thiophen-2-yl)azetidin-3-yl isoindoline-1,3-dione (**3e**).* Brown solid (82%); mp 163 °C; IR (KBr) 2958, 2927, 2854, 1772, 1718, 1593, 1465, 1394, 1287, 1217, 1120, 1073, 1034, 962, 823, 713 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.81 (d, *J*=2.70 Hz, 1H), 6.19 (d, *J*=2.64 Hz, 1H), 6.90 (dd, *J*=3.72 Hz and 1.26 Hz, 1H), 7.16 (d, *J*=3.48 Hz, 1H), 7.28 (d, *J*=4.86 Hz, 1H), 7.62–8.00 (m, 15H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 59.50, 62.13,

118.15, 120.92, 123.09, 123.48, 123.70, 123.91, 123.97, 124.44, 126.71, 126.89, 126.93, 127.20, 127.40, 127.55, 127.79, 128.09, 128.22, 128.33, 128.60, 130.25, 130.46, 131.49, 131.81, 132.19, 134.49, 134.70, 139.06, 163.72, 167.05. Anal. calcd for $C_{33}H_{20}N_2O_3S$: C, 75.56; H, 3.84; N, 5.34. Found: C, 75.48; H, 3.81; N, 5.25.

*4.2.8. (±)-trans-1-(Chrysen-6-yl)-2-oxo-4-(pyridin-2-yl)azetidin-3-yl isoindoline-1,3-dione (**3f**).* Yellow solid (73%); mp 224 °C; IR (KBr) 1767, 1716, 1618, 1440, 1393, 1107, 1075, 910,753, 713 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.01 (d, J=1.98 Hz, 1H), 6.04 (d, J=1.98 Hz, 1H), 7.19–8.79 (m, 19H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 59.78, 64.07, 117.98, 120.88, 122.55, 123.15, 123.41, 123.70, 123.87, 123.94, 124.57, 126.69, 126.89, 127.18, 127.39, 127.63, 127.98, 128.05, 128.27, 128.55, 130.22, 131.10, 131.45, 131.90, 132.15, 134.45, 134.59, 137.04, 150.49, 155.00, 164.23, 167.18. Anal. calcd for $C_{34}H_{21}N_3O_3$: C, 78.60; H, 4.07; N, 8.09. Found: C, 78.48; H, 3.99; N, 8.02.

*4.2.9. (±)-trans-1-(Chrysen-6-yl)-2-(ferrocenyl)-4-oxoazetidin-3-yl isoindoline-1,3-dione (**3g**).* Brown solid (77%); mp 158 °C; IR (KBr) 3060, 2919, 1774, 1720, 1656, 1583, 1466, 1381, 1302, 1107, 946, 876, 763, 715 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 3.89 (s, 5H), 4.10 (m, 1H), 4.14 (m, 1H), 4.24 (m, 1H), 4.31 (m, 1H), 5.69 (d, J=1.98 Hz, 1H), 5.98 (d, J=1.86 Hz, 1H), 7.65–8.89 (m, 15H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 65.72, 68.57, 68.67, 69.03, 69.43, 70.84, 82.63, 110.28, 117.97, 119.82, 120.92, 123.00, 123.81, 123.93, 126.82, 127.01, 127.11, 127.47, 127.82, 127.99, 128.13, 128.69, 130.63, 131.54, 132.28, 164.27, 168.49. Anal. calcd for $C_{39}H_{26}FeN_2O_3$: C, 74.77; H, 4.18; N, 4.47. Found: C, 74.68; H, 4.10; N, 4.36.

The optically pure 3-phthalimido β-lactams (**9a** and **9b**) were synthesized following a reported procedure from our laboratory.[27] The physical and spectral data are of the compounds **9a** and **9b** are as follows:

*4.2.10. 2-((2R,3R)-2-((S)-2,2-Dimethyl-1,3-dioxolan-4-yl)-4-oxo-1-phenylazetidin-3-yl)isoindoline-1,3-dione (**9a**).* Yellowish brown crystalline solid (69%); mp 84 °C; IR (KBr) 3357, 2980, 1766, 1717, 1601, 1500, 1382, 1207, 1065, 876, 717, 682 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 1.41 (s, 3H), 1.51 (s, 3H), 3.47 (dd, J=7.62, 1.68 Hz, 1H), 3.68 (dd, J=7.50, 1.92 Hz, 1H), 4.44 (m, 2H), 5.48 (d, J=5.64 Hz, 1H), 7.07–7.32 (m, 5H), 7.74–7.86 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 25.29, 26.43, 54.37, 62.76, 65.94, 75.27, 110.19, 115.21, 118.27, 124.15, 124.74, 128.80, 134.93, 137.65, 161.24, 167.02. Anal. calcd for $C_{22}H_{20}N_2O_5$: C, 67.34; H, 5.14; N, 7.14. Found: C, 67.21; H, 5.06; N, 7.10.

*4.2.11. 2-((2R,3R)-2-((S)-2,2-Dimethyl-1,3-dioxolan-4-yl)-1-(4-methoxyphenyl)-4-oxoazetidin-3-yl)isoindoline-1,3-dione (**9b**).* Pale yellow crystalline solid (72%); mp 160 °C; IR (KBr) 3491, 2986, 1754, 1717, 1512, 1383, 1244, 1069, 835, 711 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 1.42 (s, 3H), 1.50 (s, 3H), 3.46 (dd, J=7.62, 1.62 Hz, 1H), 3.68 (dd, J=7.53, 1.62 Hz, 1H), 3.74 (s, 3H), 4.38 (dd, J=7.23, 3.06 Hz, 1H), 4.44 (, 1H), 5.46 (d, J=5.70 Hz, 1H), 6.83 (d, J=9.12 Hz, 2H), 7.66 (d, J=9.12 Hz, 2H), 7.73 (m, 2H), 7.84 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 25.05, 26.59, 54.42, 55.51, 62.86, 65.93, 75.88, 110.16, 114.07, 119.78, 124.11, 131.15, 131.33, 134.90, 156.68, 160.69, 167.06. Anal. calcd for $C_{23}H_{22}N_2O_6$: C, 65.39; H, 5.25; N, 6.63. Found: C, 65.31; H, 5.18; N, 6.59.

4.3. General procedure for the synthesis of 3-amino β-lactam from 3-phthalimido β-lactam

A representative experimental procedure is described as follow. A solution consisting of 3-phthalimido β-lactam (1 mmol) in anhydrous ethyl alcohol (5 mL) was added ethylenediamine (2 mmol) at room temperature. This mixture was stirred at room temperature and the progress of the reaction was monitored by TLC. After completion of the reaction (15 min–1 h) the ethanol was removed by rotavapor and the crude mass was dissolved in ethyl acetate (25 mL). The solution was washed with brine and water successively (10 mL each), and dried over anhydrous sodium sulfate. The pure products were obtained via column chromatography over silica gel using ethyl acetate–hexanes as the eluent.

*4.3.1. (±)-cis-3-Amino-1,4-diphenylazetidin-2-one (**4a**).* Brown solid (88%); mp 152 °C; IR (KBr) 3292, 1751, 1647, 1535, 1455, 1306, 754 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 4.52 (d, J=5.48 Hz, 1H), 5.29 (d, J=5.48 Hz, 1H), 6.91 (s, 2H), 7.30–7.46 (m, 10H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 61.76, 64.55, 117.42, 124.14, 125.85,127.64, 128.20, 129.08, 130.42, 135.77, 168.06. Anal. calcd for $C_{15}H_{14}N_2O$: C, 75.61; H, 5.92; N, 11.76. Found: C, 75.53; H, 5.81; N, 11.67.

*4.3.2. (±)-cis-3-Amino-1-(4-methoxyphenyl)-4-phenylazetidin-2-one (**4b**).* Light yellow solid (79%); mp 137 °C; IR (KBr) 3364, 2824, 1732, 1515, 1493, 1395, 1297, 1178, 1106, 832, 748, 603 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 3.75 (s, 3H), 4.60 (d, J=5.46 Hz, 1H), 5.23 (d, J=5.46 Hz, 1H), 6.80 (s, 2H), 7.23–7.41 (m, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.45, 62.15, 66.68, 114.37, 118.68, 125.91, 127.03, 128.56, 130.95, 134.41, 156.18, 167.37. Anal. calcd for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44. Found: C, 71.49; H, 5.93; N, 10.36.

*4.3.3. (±)-trans-3-Amino-1,4-diphenylazetidin-2-one (**5a**).* Yellow solid (83%); mp 146 °C; IR (KBr) 3095, 1755, 1597, 1501, 1383, 1138, 691 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 4.02 (d, J=2.10 Hz, 1H), 4.66 (d, J=1.86 Hz, 1H), 6.87 (s, 2H), 7.34–7.49 (m, 10H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 66.57, 69.89, 117.51, 124.32, 126.29,127.99, 128.71, 129.63, 131.90, 136.25, 169.42. Anal. calcd for $C_{15}H_{14}N_2O$: C, 75.61; H, 5.92; N, 11.76. Found: C, 75.55; H, 5.86; N, 11.62.

*4.3.4. (±)-trans-3-Amino-1-(4-methoxyphenyl)-4-phenylazetidin-2-one (**5b**).* Yellow solid (81%); mp 122 °C; IR (KBr) 3280, 1725, 1453, 1395, 1246, 1106, 914, 823, 698, 522 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 3.73 (s, 3H), 4.04 (d, J=2.10 Hz, 1H), 4.64 (d, J=2.04 Hz, 1H), 6.78 (s, 2H), 7.21–7.39 (m, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.41, 63.78, 69.91, 114.12, 118.72, 125.76, 127.00, 128.14, 130.73, 136.95, 156.04, 167.10. Anal. calcd for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44. Found: C, 71.65; H, 6.10; N, 10.39.

*4.3.5. (±)-trans-3-Amino-1-(chrysen-6-yl)-4-phenylazetidin-2-one (**5c**).* Yellow solid (87%); mp 132 °C; IR (KBr) 3381, 1741, 1707, 1647, 1593, 1541, 1439, 1393, 1309, 837, 756 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 4.37 (d, J=1.61 Hz, 1H), 5.27 (d, J=1.59 Hz, 1H), 7.21–7.95 (m, 13H), 8.37–8.75 (m, 5H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 68.13, 68.44, 114.38, 120.90, 122.82, 123.51, 124.63, 126.25, 126.62, 126.75, 126.76, 127.01, 127.31, 127.46, 127.55, 128.60, 128.63, 129.02, 130.01, 131.49, 131.52, 132.20, 136.84, 169.40. Anal. calcd for $C_{27}H_{20}N_2O$: C, 83.48; H, 5.19; N, 7.21. Found: C, 83.45; H, 5.14; N, 7.16.

*4.3.6. (±)-trans-3-Amino-1-(chrysen-6-yl)-4-(4-methoxyphenyl) azetidin-2-one (**5d**).* Yellow solid (86%); mp 128 °C; IR (KBr) 32, 491, 741, 1594, 1512, 1438, 1394, 1305, 1246, 1174, 1022, 817, 755 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 3.65 (s, 1H), 4.34 (d, J=1.42 Hz, 1H), 5.19 (d, J=1.42 Hz, 1H), 6.76 (d, J=8.52 Hz, 2H), 7.34 (d, J=8.52 Hz, 2H), 7.57–8.71 (m, 13H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.19, 67.90, 68.37, 114.41, 114.56, 120.87, 122.83, 123.47, 124.59, 126.57, 126.70, 127.07, 127.22, 128.56, 128.68, 130.00, 131.41, 131.43, 132.17, 159.82, 169.54. Anal. calcd for $C_{28}H_{22}N_2O_2$: C, 80.36; H, 5.30; N, 6.69. Found: C, 80.31; H, 5.23; N, 6.62.

*4.3.7. (±)-trans-3-Amino-1-(chrysen-6-yl)-4-(thiophen-2-yl)azetidin-2-one (**5e**).* Yellow solid (89%); mp 184 °C; IR (KBr) 1740, 1594,

1438, 1395, 1118, 817, 755 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 4.54 (d, J=2.16 Hz, 1H), 5.49 (d, J=2.04 Hz, 1H), 6.85 (dd, J=3.66 Hz and 1.20 Hz, 1H), 7.11 (d, J=3.42, 1H), 7.16 (d, J=4.92 Hz, 1H), 7.63–8.75 (m, 13H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 64.51, 69.45, 109.79, 110.10, 115.77, 120.91, 122.89, 123.51, 124.40, 125.88, 126.65, 126.66, 126.81, 126.83, 127.19, 127.32, 127.42, 127.61, 127.68, 128.62, 131.46, 132.21, 140.39, 168.98. Anal. calcd for $C_{25}H_{18}N_2OS$: C, 76.12; H, 4.60; N, 7.10. Found: C, 76.01; H, 4.53; N, 7.02.

*4.3.8. (±)-trans-3-Amino-1-(chrysen-6-yl)-4-(pyridin-2-yl)azetidin-2-one (**5f**).* Light yellow solid (80%); mp 154 °C; IR (KBr) 3366, 1742, 1591, 1513, 1437, 1395, 1309, 860, 816, 755 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 4.60 (d, J=1.92 Hz, 1H), 5.40 (d, J=1.92 Hz, 1H), 7.10–8.76 (m, 17H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 67.21, 68.86, 115.03, 120.84, 121.14, 122.98, 123.37, 123.45, 124.65, 124.79, 125.12, 125.77, 126.66, 126.78, 126.81, 127.14, 127.32, 127.55, 128.32, 128.55, 131.99, 132.17, 137.00, 150.05, 156.34, 169.33. Anal. calcd for $C_{26}H_{19}N_3O$: C, 80.18; H, 4.92; N, 10.79. Found: C, 80.11; H, 4.83; N, 10.75.

*4.3.9. (±)-trans-3-Amino-1-(chrysen-6-yl)-4-(ferrocenyl)azetidin-2-one (**5g**).* Yellow solid (79%); mp 205 °C; IR (KBr) 3077, 1740, 1593, 1513, 1439, 1393, 1315, 1243, 1104, 818, 796 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 4.08 (s, 5H), 4.14 (m, 1H), 4.16 (m, 1H), 4.25 (m, 1H), 4.28 (m, 1H), 4.46 (d, J=1.86 Hz, 1H), 5.00 (d, J=1.86 Hz, 1H), 7.56–8.79 (m, 13H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 65.69, 65.99, 66.85, 68.50, 68.68, 69.03, 69.20, 69.57, 83.73, 116.63, 120.98, 122.98, 123.61, 124.37, 126.69, 126.80, 126.88, 17.31, 127.61, 127.71, 127.82, 128.67, 130.19, 131.34, 131.49, 132.28, 170.00. Anal. calcd for $C_{31}H_{24}FeN_2O$: C, 75.01; H, 4.87; N, 5.64. Found: C, 74.89; H, 4.76; N, 5.52.

*4.3.10. (3R,4R)-3-Amino-4-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)-1-phenylazetidin-2-one (**10a**).* White amorphous solid (70%); mp 177 °C; IR (KBr) 3276, 2982, 1757, 1645, 1539, 1372, 1304, 1259, 1212, 1154, 1065, 752, 692 cm^{-1}; ^1H NMR (600 MHz, DMSO) δ 1.26 (s, 3H), 1.47 (s, 3H), 3.63 (m, 1H), 3.79 (m, 1H), 3.92 (t, J=5.80 Hz, 1H), 4.23 (m, 1H), 4.43 (dd, J=5.64, 2.40 Hz, 1H), 7.36–7.65 (m, 5H); ^{13}C NMR (150 MHz, DMSO) δ 24.95, 26.40, 60.01, 62.94, 65.19, 76.30, 108.98, 117.65, 127.68, 128.67, 129.33, 138.05, 167.06. Anal. calcd for $C_{14}H_{18}N_2O_3$: C, 64.10; H, 6.92; N, 10.68. Found: C, 64.01; H, 6.88; N, 10.65.

*4.3.11. (3R,4R)-3-Amino-4-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)-1-(4-methoxyphenyl)azetidin-2-one (**10b**).* White crystalline solid (78%); mp 149 °C; IR (KBr) 3273, 2972, 1736, 1642, 1514, 1377, 1299, 1252, 1050 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 1.27 (s, 3H), 1.36 (s, 3H), 3.72 (s, 3H), 3.73 (m, 1H), 3.78 (dd, J=7.14, 2.04 Hz, 1H), 4.13 (t, J=5.82 Hz, 1H), 4.23–4.29 (m, 2H), 6.78 (d, J=9.06 Hz, 2H), 7.47 (d, J=9.06 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 25.17, 26.49, 55.46, 60.60, 61.24, 66.91, 76.56, 109.73, 114.14, 119.96, 131.34, 156.43, 168.43. Anal. calcd for $C_{15}H_{20}N_2O_4$: C, 61.63; H, 6.90; N, 9.58. Found: C, 61.47; H, 6.81; N, 9.46.

4.4. General procedure for the synthesis of 3-pyrrole substituted β-lactam from 3-amino substituted β-lactam

The substrate (3-amino substituted β-lactam, 1.0 mmol), 2,5-dimethoxytetrahydrofuran (1.2 mmol), and bismuth nitrate pentahydrate (24 mg, 5 mol %) were mixed together in a microwave vial with a magnetic stir bar. The mixture was irradiated in an automated microwave (CEM Corporation) and the progress of the reaction was monitored by TLC. After completion of the reaction (Table 4) diethyl ether (10 mL) was added to the reaction mixture and the organic layer was washed with saturated sodium bicarbonate solution, brine, and water successively. It was dried over anhydrous sodium sulfate and the solvent was removed under reduced pressure. The crude mass was purified through a small silica gel column using ethyl acetate/hexanes as eluent.

*4.4.1. (±)-cis-1,4-Diphenyl-3-(1H-pyrrol-1-yl)azetidin-2-one (**6a**).* White solid (93%); mp 158 °C; IR (KBr) 3247, 2913, 1759, 1516, 1450, 1291, 1115, 712 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.43 (d, J=5.41 Hz, 1H), 5.74 (d, J=5.40 Hz, 1H), 5.87 (t, J=2.04 Hz, 2H), 6.47 (t, J=2.04, 2H), 7.14–7.42 (m, 10H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 62.12, 68.43, 109.08, 117.90, 120.44, 125.05, 126.77, 128.60, 129.59, 132.67, 137.84, 162.03. Anal. calcd for $C_{19}H_{17}N_2O$: C, 79.14; H, 5.59; N, 9.72. Found: C, 79.01; H, 5.52; N, 9.63.

*4.4.2. (±)-trans-1,4-Diphenyl-3-(1H-pyrrol-1-yl)azetidin-2-one (**7a**).* White solid (96%); mp 155 °C; IR (KBr) 3128, 2945, 2914, 1750, 1593, 1493, 1447, 1375, 1317, 1222, 1133, 1084, 961, 896, 728, 705 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 4.97 (d, J=1.92 Hz, 1H), 5.12 (d, J=2.04 Hz, 1H), 6.26 (t, J=1.98 Hz, 2H), 6.77 (t, J=1.92 Hz, 2H), 7.09–7.42 (m, 10H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 65.36, 73.25, 110.08, 117.68, 119.58, 124.78, 125.89, 126.01, 129.14, 129.48, 135.68, 136.78, 161.93. Anal. calcd for $C_{19}H_{17}N_2O$: C, 79.14; H, 5.59; N, 9.72. Found: C, 79.08; H, 5.56; N, 9.65.

*4.4.3. (±)-cis-1-(4-Methoxyphenyl)-4-phenyl-3-(1H-pyrrol-1-yl) azetidin-2-one (**6b**).* White crystalline solid (88%); mp 162 °C; IR (KBr) 3060, 2966, 1742, 1510, 1488, 1388, 1297, 1242, 1172, 1092, 808, 725, 692 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 3.77 (s, 3H), 5.39 (d, J=5.28 Hz, 1H), 5.76 (d, J=5.34 Hz, 1H), 5.88 (t, J=2.04 Hz, 2H), 6.47 (t, J=1.98 Hz, 2H), 6.83 (d, J=9.0 Hz, 2H), 7.11–7.27 (m, 5H), 7.36 (d, J=9.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.48, 62.02, 68.23, 109.04, 114.48, 118.79, 120.17, 126.65, 128.31, 128.53, 130.69, 132.55, 156.66, 161.07. Anal. calcd for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.31; H, 5.63; N, 8.72.

*4.4.4. (±)-trans-1-(4-Methoxyphenyl)-4-phenyl-3-(1H-pyrrol-1-yl) azetidin-2-one (**7b**).* White crystalline solid (95%); mp 145 °C; IR (KBr) 3126, 2958, 2931, 1757, 1728, 1514, 1463, 1450, 1382, 1321, 1288, 1258, 1135, 1091, 1069, 1036, 827, 740, 727 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 3.74 (s, 3H), 4.93 (d, J=2.04 Hz, 1H), 5.10 (d, J=2.04 Hz, 1H), 6.25 (t, J=2.16 Hz, 2H), 6.76 (t, J=2.10 Hz, 2H), 6.80 (d, J=2.16 Hz, 1H), 6.81 (d, J=2.22 Hz, 1H), 7.28–7.40 (m, 7H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.45, 65.44, 73.24, 110.00, 114.47, 119.02, 119.56, 125.95, 129.10, 129.44, 130.87, 135.74, 156.65, 161.29. Anal. calcd for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.36; H, 5.59; N, 8.74.

*4.4.5. (+)-trans-1-(Chrysen-6-yl)-4-phenyl-3-(1H-pyrrol-1-yl)azetidin-2-one (**7c**).* White solid (89%); mp 124 °C; IR (KBr) 2919, 2353, 2323, 1762, 1707, 1593, 1488, 1455, 1438, 1387, 1346, 1314, 1092, 1070, 817 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.44 (d, J=2.02 Hz, 1H), 5.54 (d, J=2.02 Hz, 1H), 6.35 (t, J=2.08 Hz, 2H), 6.96 (t, J=2.12 Hz, 2H), 7.27–7.98 (m, 11H), 8.41–8.81 (m, 11H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 67.51, 7191, 110.25, 115.53, 119.74, 120.87, 122.85, 123.72, 124.30, 126.33, 126.79, 126.92, 127.03, 127.46, 127.50, 127.72, 127.92, 128.67, 129.21, 129.35, 130.01, 130.89, 131.61, 132.24, 135.71, 163.46. Anal. calcd for $C_{31}H_{22}N_2O$: C, 84.91; H, 5.06; N, 6.39. Found: C, 84.77; H, 4.97; N, 6.31.

*4.4.6. (±)-trans-1-(Chrysen-6-yl)-4-(4-methoxyphenyl)-3-(1H-pyrrol-1-yl)azetidin-2-one (**7d**).* Light yellow solid (91%); mp 160 °C; IR (KBr) 3099, 2990, 2357, 1755, 1603, 1509, 1478, 1439, 1232, 1173, 1142, 1095, 1017, 958, 821, 743 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 3.71 (s, 3H), 5.35 (d, J=2.22 Hz, 1H), 5.41 (d, J=2.16 Hz, 1H), 6.27 (t, J=2.10 Hz, 2H), 6.74 (d, J=8.64 Hz, 2H), 6.88 (t, J=2.10 Hz, 2H), 7.31 (d, J=8.58 Hz, 2H), 7.63–8.82 (m, 11H); ^{13}C NMR (150 MHz, $CDCl_3$)

δ 55.27, 67.35, 71.99, 110.17, 114.75, 115.77, 119.74, 120.87, 122.88, 123.71, 124.27, 126.77, 126.91, 127.00, 127.01, 127.45, 127.48, 127.69, 127.77, 127.88, 128.66, 130.03, 130.81, 131.59, 132.24, 160.28, 163.63. Anal. calcd for $C_{32}H_{24}N_2O_2$: C, 82.03; H, 5.16; N, 5.98. Found: C, 81.96; H, 5.11; N, 5.90.

*4.4.7. (±)-trans-1-(Chrysen-6-yl)-3-(1H-pyrrol-1-yl)-4-(thiophen-2-yl)azetidin-2-one (**7e**).* Yellow solid (88%); mp 150 °C; IR (KBr) 1762, 1593, 1487, 1438, 1389, 1371, 816 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.58 (d, *J*=2.04 Hz, 1H), 5.76 (d, *J*=1.98 Hz, 1H), 6.36 (t, *J*=1.92 Hz, 2H), 6.88 (dd, *J*=3.78 Hz, 1.08 Hz, 1H), 6.98 (t, *J*=2.04 Hz, 2H), 7.11 (d, *J*=3.36 Hz, 1H), 7.23 (d, *J*=4.98 Hz, 1H), 7.61–8.79 (m, 11H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 63.87, 72.90, 110.28, 110.36, 116.99, 119.74, 119.83, 120.85, 122.91, 123.73, 124.02, 126.56, 126.81, 126.99, 127.08, 127.29, 127.32, 127.42, 127.50, 128.01, 128.12, 128.66, 130.08, 130.19, 131.56, 132.22, 138.95, 163.22. Anal. calcd for $C_{29}H_{20}N_2OS$: C, 78.35; H, 4.53; N, 6.30. Found: C, 78.21; H, 4.45; N, 6.24.

*4.4.8. (±)-trans-1-(Chrysen-6-yl)-4-(pyridin-2-yl)-3-(1H-pyrrol-1-yl)azetidin-2-one (**7f**).* White solid (90%); mp 224 °C; IR (KBr) 3057, 1756, 1591, 1488, 1471, 1437, 1393, 1318, 1141, 1095, 1070, 816, 761 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.56 (d, *J*=1.68 Hz, 1H), 5.88 (d, *J*=1.68 Hz, 1H), 6.35 (t, *J*=1.92 Hz, 2H), 7.02 (t, *J*=1.95 Hz, 2H), 7.16–8.78 (m, 15H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 68.18, 70.19, 110.10, 117.45, 119.98, 120.82, 122.63, 123.91, 124.10, 126.96, 127.03, 127.45, 127.51, 127.88, 128.02, 128.62, 130.10, 130.76, 131.49, 132.18, 136. 94, 150.54, 154.62, 163.99. Anal. calcd for $C_{30}H_{21}N_3O$: C, 81.98; H, 4.82; N, 9.56. Found: C, 81.89; H, 4.76; N, 9.49.

*4.4.9. (±)-trans-1-(Chrysen-6-yl)-4-(ferrocenyl)-3-(1H-pyrrol-1-yl) azetidin-2-one (**7g**).* Orange crystalline solid (89%); mp 208 °C; IR (KBr) 2360, 1754, 1593, 1490, 1439, 1381, 1314, 1105, 819, 756, 727 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 3.82 (s, 5H), 4.02 (m, 1H), 4.07 (m, 1H), 4.16 (m, 1H), 4.24 (m, 1H), 5.29 (d, *J*=2.28 Hz, 1H), 5.43 (d, *J*=2.28 Hz, 1H), 6.32 (t, *J*=2.10 Hz, 2H), 6.98 (d, *J*=2.28 Hz, 2H), 7.48–8.76 (m, 11H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 65.72, 68.58, 68.68, 69.03, 69.43, 70.84, 82.63, 110.28, 117.96, 119.83, 120.92, 123.00, 123.81, 123.93, 126.82, 127.01, 127.10, 127.47, 127.82, 127.99, 128.13, 128.69, 130.15, 130.64, 131.54, 132.28, 164.27. Anal. calcd for $C_{35}H_{26}FeN_2O$: C, 76.93; H, 4.80; N, 5.13. Found: C, 76.81; H, 4.69; N, 5.06.

*4.4.10. (3R,4R)-4-((S)-2,2-Dimethyl-1,3-dioxolan-4-yl)-1-phenyl-3-(1H-pyrrol-1-yl)azetidin-2-one (**11a**).* Pale yellow crystalline solid (92%); mp 131 °C; IR (KBr) 2918, 1766, 1593, 1570, 1370, 1204, 1095, 822, 730, 691 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 1.17 (s, 3H), 1.40 (s, 3H), 2.88 (t, *J*=7.02 Hz, 1H), 3.26 (m, 1H), 4.05 (dd, *J*=11.01, 8.16 Hz, 1H), 4.29 (m, 1H), 5.44 (d, *J*=5.58 Hz, 1H), 6.16 (s, 2H), 6.62 (s, 2H), 7.09 (t, *J*=7.38 Hz, 1H), 7.29 (t, *J*=7.80 Hz, 2H), 7.73 (d, *J*=8.22 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 25.12, 26.52, 62.91, 64.82, 65.76, 77.21, 109.81, 110.55, 118.78, 120.69, 124.99, 128.98, 137.55, 162.19. Anal. calcd for $C_{18}H_{20}N_2O_3$: C, 69.21; H, 6.45; N, 8.97. Found: C, 69.11; H, 6.40; N, 8.90.

*4.4.11. (3R,4R)-4-((S)-2,2-Dimethyl-1,3-dioxolan-4-yl)-1-(4-methoxyphenyl)-3-(1H-pyrrol-1-yl)azetidin-2-one (**11b**).* White crystalline solid (94%); mp 142 °C; IR (KBr) 3122, 2986, 1738, 1514, 1385, 1237, 832, 736 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 1.18 (s, 3H), 1.39 (s, 3H), 2.87 (dd, *J*=7.74, 3.24 Hz, 1H), 3.26 (t, *J*=8.22 Hz, 1H), 3.74 (s, 3H), 4.03 (dd, *J*=11.37, 7.32 Hz, 1H), 4.23 (dd, *J*=7.08, 3.12 Hz, 1H), 5.41 (d, *J*=5.52 Hz, 1H), 6.16 (s, 2H), 6.61 (s, 2H), 6.82 (d, *J*=8.88 Hz, 2H), 7.67 (d, *J*=8.88 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 25.15, 26.54, 55.50, 63.04, 64.85, 65.78, 77.20, 109.78, 110.49, 114.09, 119.81, 120.68, 131.02, 156.84, 161.61. Anal. calcd for $C_{19}H_{22}N_2O_4$: C, 66.65; H, 6.48; N, 8.18. Found: C, 66.49; H, 6.36; N, 8.04.

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Supplementary data

IR, ^1H and ^{13}C NMR spectra of compounds **7a**–**g**, **6b** and **11b** can be found online. Supplementary data related to this article can be found online at http://dx.doi.org/10.1016/j.tet.2012.06.009.

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