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Synthesis of some new polycyclic aromatic monocyclic β-lactams

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Abstract

In this paper the synthesis of some new polyaromatic monocyclic β-lactams has been reported. These cycloadducts have been synthesized by the [2+2] ketene-imine cycloaddition reaction known as the Staudinger reaction. All of the products have been fully characterized by IR, ^{1}H-NMR, ^{13}C-NMR, mass spectroscopy and elemental analyses. The X-ray crystal structure of a cis β-lactam has been also presented. The cycloaddition reaction was found to be totally diastereoselective leading exclusively to the formation of the *cis*-β-lactams for **3c-e, 3g, 3i-k, 3p** and the rest were found to be totally *trans.*

Keywords: 2-azetidinone; polyaromatic; Schiff bases; [2+2] cycloaddition; Staudinger reaction

1. Introduction

2-Azetidinone (β-lactam) skeleton is the key pharmacophore of β-lactam antibiotics, the most widely employed class of antibacterial agents (Setti et al., 1998; Georg et al., 1993; Neuhaus et al., 1992; Page et al., 1992). The importance of biologically active β-lactam antibiotics led to the development of many novel methods for the construction of substituted 2-azetidinones (Troisi et al., 2006; Singh et al., 2003; Katritzky et al., 1996; Brown et al., 1989; Isaacs N S., 1976; Mihovilovic et al., 2005; Shirode et al., 2005). Banik and his coworkers have been engaged in the synthesis and biological evaluation of compounds in which a polycyclic aromatic ring is present (Becker et al., 1998). During the course of this study, we became interested in the synthesis of β-lactam bound to a polyaromatic ring. Although there are many methods known for the construction of the β-lactam rings, the Staudinger reaction is still the most frequently used and is considered to be the most effective (Staudinger H., 1907). Banik et al have described the asymmetric synthesis of a novel anticancer β-lactam using Staudinger reaction with chiral carbohydrate as the ketene component with an achiral imine (Banik et al., 2010). Polyaromatics have been found to slow or inhibit tumor cell growth, and the 4-alkylidene beta-lactams are capable of inhibiting matrix metalloproteinases and leukocyte elactase activity (Kuhn et al., 2004).

Synthesis and evaluation of β-lactams are a promising area for further development in anticancer research. Banik et al have presented stereoselective synthesis of novel beta-lactams using polyaromatic imines following the Staudinger reaction (Banik et al., 2003; Bandyopadhyay et al., 2010). In our previous article, some new mono-and bis-polycyclic aromatic spiro-β-lactams and bis-non spiropolycyclic aromatic β-lactams have been reported from imines derived from anthracene-9-carbaldehyde, 2-naphtaldehyde and a ketene derived from 9H-xanthene-9- carboxylic acid and phenoxyacetic acid by a [2+2] cycloaddition reaction (Jarrahpour et al., 2010). Reactions of polyaromatic imines with acid chlorides in the presence of triethylamine produced *trans*-β-lactams (Bandyopadhyay et al., 2009). This paper describes the synthesis of β-lactams bearing polyaromatics as potential anticancer agents.

2. Results and Discussion

Polycyclic aromatic aldimines **1a-q** were prepared in quantitative yield by condensation of polycyclic aromatic amines with polycyclic aromatic aldehydes in refluxing ethanol. The formation of Schiff bases were readily established from their spectral data. Treatment of Schiff bases **1a-q** with phenoxy and methoxy ketenes derived from phenoxy and methoxy acetyl chlorides **2** in the presence of triethylamine afforded *cis* or *trans*-2-azetidinones **3a-q** (Scheme 1, Table 1).

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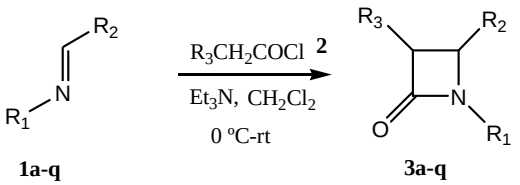
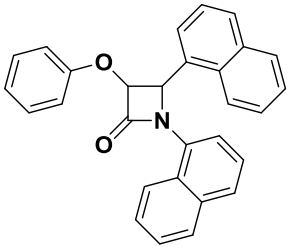
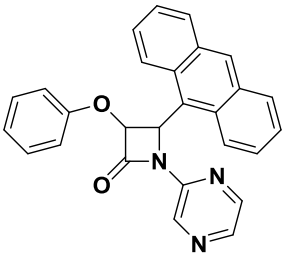
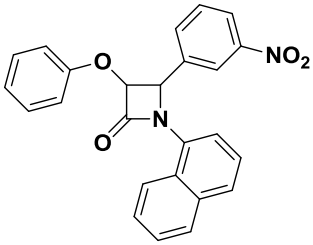
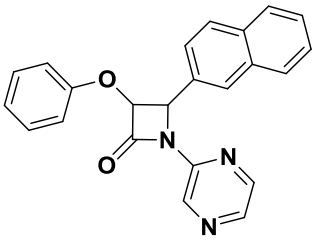
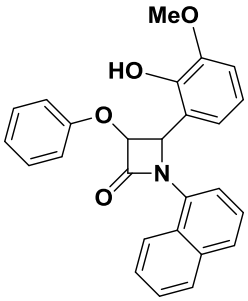
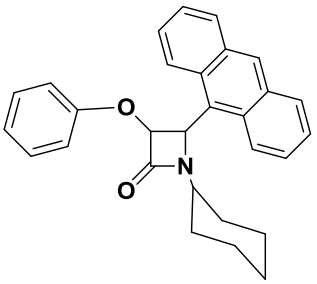
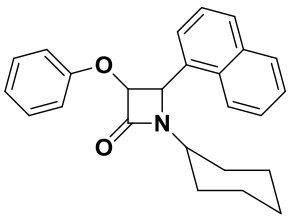
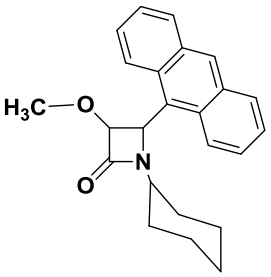


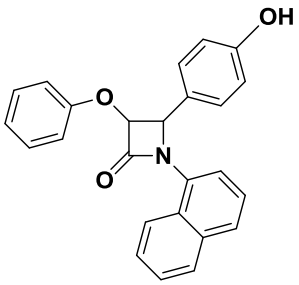
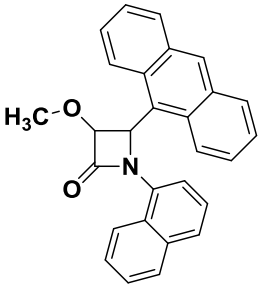
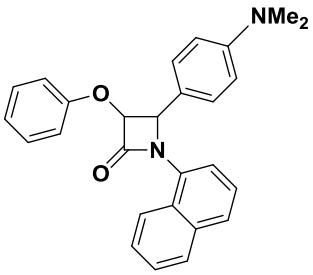
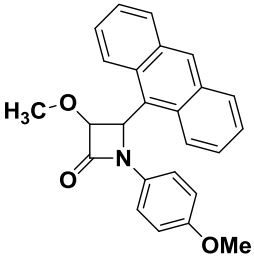
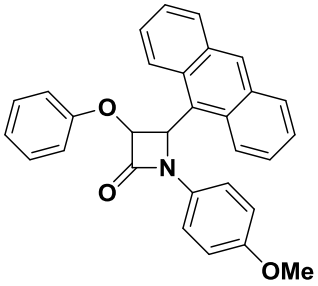
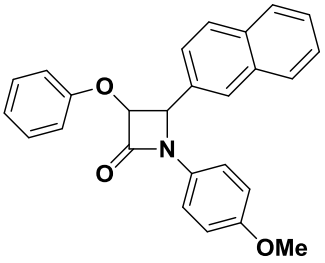
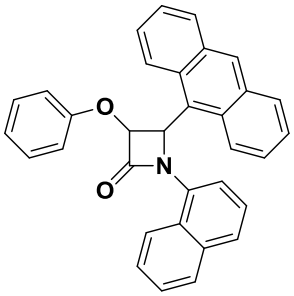
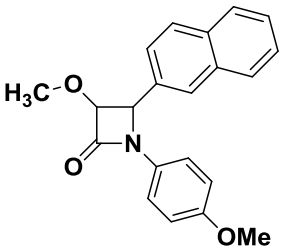
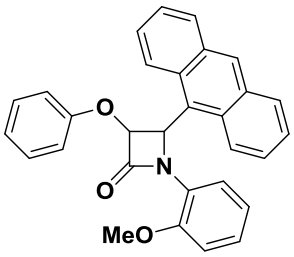
1a-q **3a-q**

Scheme 1. Synthesis of *cis* or *trans*-β-lactam derivatives **3a–q**.

The *cis* and *trans* stereochemistries of 2-azetidinones were deduced from the coupling constants of H-3 and H-4 ($J_{3,4}$>4.0 Hz for the cis and $J_{3,4}$<3.0 Hz for the trans stereoisomer) (Jarrahpour et al., 2014). Unfortunately, the β-lactams **3a–q** were not suitable for crystallographic studies except for one which is shown in Fig. 1, but all the cycloadducts were fully characterized by spectral and elemental analyses. Typically, for compound **3a** the ^{1}H-NMR spectrum exhibited the β-lactam ring hydrogen H-4 as a doublet at 5.03 ppm (J = 1.55 Hz) and H-3 as a doublet at 5.53 ppm (J = 1.55 Hz).

Table 1. Isolated yields for *cis* or *trans*-β-lactam derivatives **3a–q**

β-lactam	Structure	Yield(%) *cis/trans* (%)	β-lactam	**Structure**	Yield(%)[a] *cis/trans* (%)
3a		35 (0:100)	**3j**		34 (100:0)
3b		32 (0:100)	**3k**		30 (100:0)
3c		55 (100:0)	**3l**		33 (0:100)
3d		60 (100:0)	**3m**		37 (0:100)

3e		50 (100:0)	**3n**		43 (0:100)
3f		51 (0:100)	**3O**		40 (0:100)
3g		27 (100:0)	**3p**		47 (100:0)
3h		38(0:100)	**3q**		38(0:100)
3i		45(100:0)			

The *cis* stereochemistry is also confirmed from the N1-deprotected β-lactam **3b**, which contains a nearly planar four-membered β-lactams ring, making dihedral angles of 67.01 and 75.21 with the phenyl and the benzene rings, respectively (Akkurt et al., 2007).

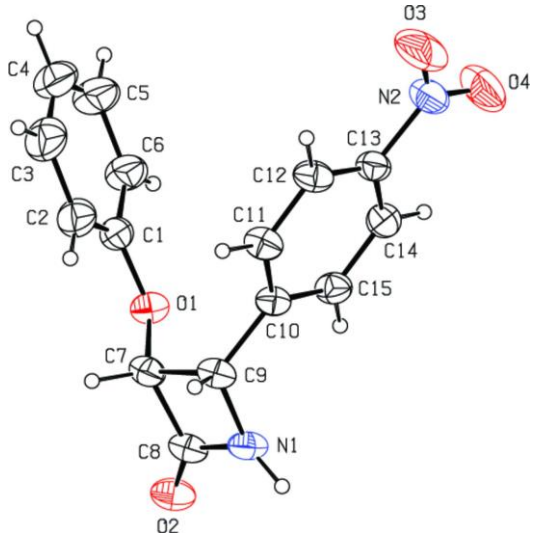


Fig. 1. The crystal structure of N1-deprotected β-lactam

3. Experimental

3.1. General

All required chemicals were purchased from Merck, Sigma Aldrich, Acros and Fluka. Dichloromethane and triethylamine were dried by distillation over CaH2 and then stored over 4Å molecular sieves. IR spectra were run on a Shimadzu FT-IR 8300 spectrophotometer. ^{1}H-NMR and ^{13}C-NMR spectra were recorded in $CDCl_3$ using a Bruker Avance DPX instrument (operating at 250 MHz for 1H and 62.9 MHz for 13C). Chemical shifts were reported in ppm (δ) downfield from TMS. All of the coupling constants (J) are in Hertz. The mass spectra were recorded on a Shimadzu GC-MS QP 1000 EX instrument. Elemental analyses were run on a Thermo Finnigan Flash EA-1112 series. Melting points were determined in open capillaries with a Buchi 510 melting point apparatus and are not corrected. Thin-layer chromatography (t.l.c.) was carried out on silica gel 254 analytical sheets obtained from Fluka. Column chromatography was performed on Merck Kieselgel (230-270 mesh).

3.2. General procedure for the preparation of imines 1a-q

A mixture of amine (1.00 mmol) and different aldehyde (1.00 mmol) was refluxed in ethanol (20 ml) for several hours. Evaporation of the solvent afforded the solid crude imines, which were used for the next step without further purification. Some of these Schiff bases were purified by recrystallization from ethanol.

3.3. General procedure for the synthesis of monocyclic β-lactams

A solution of the corresponding acetyl chloride (1.3 mmol) in dry CH_2Cl_2 (10 mL) was slowly added to a solution of Schiff bases and triethylamine (2.6 mmol) in CH_2Cl_2 (15 mL) at 0^{o}C. The reaction mixture was then allowed to warm to room temperature, stirred overnight and then it was washed with saturated sodium bicarbonate solution (20 mL), brine (20 mL), and water, then dried (Na_2SO_4) and the solvent was evaporated to give the crude product which was then purified by column chromatography over silica gel or recrystallized from ethyl acetate.

3.3.1. 1-(Naphthalen-1-yl)-4-(naphthalen-2-yl)-3-phenoxyazetidin-2-one 3a

IR (KBr, cm^{-1}): 1743 (β-lactam, C=O), ^{1}H-NMR ($CDCl_3$), δ (ppm): 5.03 (H_4, d, 1H, *J* = 1.55), 5.53 (H_3, d, 1H, *J* = 1.55), 6.98-7.89 (ArH, m, 19H), ^{13}C-NMR δ (ppm): 64.99 (C4, β-lactam), 86.18 (C3, β-lactam), 115.62-129.73 (aromatic carbons), 157.00 (Ph-O-C_3), 162.50 (CO, β-lactam), MS (m/z, 55%): 416 (M+1), 415 (M), 281, 246, 169, 141, 140, 127, 77, 69, Anal. Calcd for $C_{29}H_{21}NO_2$: C, 83.83; H, 5.09; N, 3.37 Found: C, 84.00; H, 4.99; N, 3.27

3.3.2. 1-(Naphthalen-1-yl)-4-(3-nitrophenyl)-3-phenoxyazetidin-2-one 3b

m.p: 165-177 ^{o}C, IR (KBr, cm^{-1}): 1730 (β-lactam, C=O), ^{1}H-NMR ($CDCl_3$), δ (ppm): 5. 32 (H_4, d, 1H, *J* =1.85), 5.49 (H_3, d, *J* = 1.85), 6.80-8.28 (ArH, m, 16H), ^{13}C-NMR δ (ppm): 60.37 (C4, β-lactam), 86.14 (C3, β-lactam), 114.71-156.90 (aromatic carbons), 163.54 (C-NO2), 166.92 (Ph-O-C_3), 171.18 (C=O), MS (m/z, 30%): 411 (M+1), 410 (M), 288, 283, 127, 122, 93, 77, 69, Anal. Calcd for: $C_{25}H_{18}N_2O_4$: C, 73.16; H, 4.42; N, 6.83 Found: C, 73.03; H, 4.35; N, 6.70.

4-(2-Hydroxy-3-methoxyphenyl)-1-(naphthalene-1-yl)-3-phenoxy azetidin-2-one 3c

m.p: 170-173 ^{o}C, IR (KBr, cm^{-1}): 1760 (β-lactam, C=O), ^{1}H-NMR ($CDCl_3$), δ (ppm): 3.76 (3H, s, O<u>C</u>H$_3$) 4.88 (1H, m, O<u>H</u>), 5.33 (H_4, d, 1H, *J* = 5.55), 5.70 (H_3, d, *J* = 5.55), 6.86-7.95 (ArH, m, 15H), ^{13}C-NMR δ (ppm): 50.55 (C_4, βlactam carbon), 57.11 (O<u>C</u>H$_3$), 88.07 (C_3, βlactam carbon), 110.63-150.86 (aromatic carbons), 159.30 (Ph-O-C_3), 165.39 (C=O), MS (m/z, 100%): 412(M+1), 411(M), 288, 285, 127, 123, 93, 78, 77, 69, 55, Anal. Calcd for $C_{26}H_{21}N_2O_4$: C, 75.90; H, 5.14; N, 3.40 Found: C, 75.82; H, 5.02; N, 3.30.

1-Cyclohexyl-4(naphthalen-2-yl)-3-phenoxyazetidin-2-one 3d

m.p: 203-207 ^{o}C, IR (KBr, cm^{-1}): 1755 (β-lactam,

C=O), ^{1}H-NMR ($CDCl_3$), δ (ppm): 1.09-1.99 (10H, m, cyclohexyl protons), 3.57 (H, m, CH-N, cyclohexyl), 4.80 (H_4, d, 1H, *J* = 4.55), 5.42 (H_3, d, 1H, *J* = 4.55), 6.70-7.79 (ArH, m, 13H), ^{13}C-NMR δ (ppm): 24.9-31.49 (cyclohexyl), 52.73 (CN, cyclohexyl), 61.43 (C4), 81.27 (C3), 115.58-133.43 (aromatic carbons), 157.05 (Ph-O-C_3), 165.61 (CO, β-lactam), MS (m/z, 100%): 372(M+1), 371(M), 246, 244, 141, 127, 125, 97, 83, 69, 56, Anal. Calcd for $C_{25}H_{25}NO_2$: C, 80.83; H, 6.78; N, 3.37 Found: C, 80.71; H, 6.65; N, 3.23.

4-(4-Hydroxyphenyl)-1-(naphthalen-1-yl)-3-phenoxyazetidin-2-one 3e

m.p: 170-172 °C, IR (KBr, cm^{-1}): 1733 (β-lactam, C=O), ^{1}H-NMR ($CDCl_3$), δ (ppm): 4.74 (1H, s, OH), 4.83 (H_4, d, 1H, *J* = 5.55), 5.53 (H_3, d, 1H, *J* = 5.55), 6.86-7.95 (ArH, m, 16H), ^{13}C-NMR δ (ppm): 60.45 (C_4, βlactam carbon), 85.97 (C_3, βlactam carbon), 114.63-148.86 (aromatic carbons), 152.36 (C-N), 158.99 (C-OH), 160.34 (Ph-O-C_3), 167.29 (C=O), MS (m/z, 50%): 382(M+1), 381(M), 247, 169, 127, 115, 94, 93, 78, 69, 55, Anal. Calcd for $C_{25}H_{19}NO_3$: C, 78.72; H, 5.02; N, 3.67 Found: C, 78.70; H, 5.05; N, 3.60.

4-(4-(Dimethylamino) phenyl)-1-(naphthalen-1-yl)-3-phenoxyazetidin-2-one 3f

m.p: 165-170 °C, IR (KBr, cm^{-1}): 1758 (β-lactam, C=O), ^{1}H-NMR ($CDCl_3$), δ (ppm): 2.88 (6H, S, N-(CH3)$_2$), 5.26 (H4, d, 1H, *J* = 1.65), 5.70 (H4, d, 1H, *J* = 1.65), 6.59-7.70 (ArH, m, 16H), ^{13}C-NMR δ (ppm): 40.57 (N-(OCH3)$_2$), 65.91 (C_4), 86.21 (C_3), 112.42-134.37 (aromatic carbons), 157.26 (Ph-O-C_3), 164.24 (C=O), MS (m/z, 40%): 409(M+1), 408(M), 346, 239, 210, 169, 134, 77, 69, 51, Anal. Calcd for $C_{27}H_{24}N_2O_2$: C, 79.39; H, 5.92; N, 6.86 Found: C, 79.35; H, 5.91; N, 6.80

4-(Anthracen-10-yl)-1-(4-methoxyphenyl)-3-phenoxy-2- azetidinone 3g

IR (KBr, cm^{-1}): 1745 (β-lactam, C=O), ^{1}H-NMR ($CDCl_3$), δ (ppm): 3.86 (3H, s, OCH3), 6.02 (H_4, d, 1H, *J* = 5.15), 6.35 (H_3, d, 1H, *J* = 5.15), 6.56-7.44 (ArH, m, 18H), ^{13}C-NMR δ (ppm): 55.06 (OCH3), 84.12 (C3, β-lactam), 111.65-134.07 (aromatic carbons), 150.51 (C-OCH3), 156.99 (Ph-O-C_3), 164.93 (CO, β-lactam), MS (m/z, 75%): 445 (M), 446 (M+1), 324, 296, 134, 121, 107, 77, 69. Anal. Calcd for $C_{30}H_{23}NO_3$: C, 80.88; H, 5.20; N, 3.14 Found: C, 80.85; H, 5.22; N, 3.10.

4-(Anthracen-10-yl)-1-(naphthalen-1-yl)-3-phenoxyazetidin-2-one 3h

m.p: 235-240 °C, IR (KBr, cm^{-1}):1788 (CO β-lactam), ^{1}H-NMR ($CDCl_3$), δ (ppm): 5.59 (H_4, d, 1H, *J* = 2.2), 6.15 (H_3, d, 1H, *J* = 2.2), 6.86-7.99 (ArH, m, 18H), ^{13}C-NMR δ (ppm): 61.75 (C4, β-lactam), 85.38 (C3, β-lactam), 115.73-131.46 (aromatic carbons), 144.00 (N-C), 157.50 (Ph-O-C_3), 167.44 (C=O), MS (m/z, 100%): 466 (M+1), 465 (M), 331, 296, 177, 169, 134, 127, 77, 69, Anal. Calcd for $C_{33}H_{23}NO_2$: C, 85.14; H, 4.98; N, 3.01 Found: C, 85.11; H, 4.95; N, 3.07

4-(Anthracen-10-yl)-1-(2-methoxyphenyl)-3-phenoxyazetidin-2-one 3i

m.p: 175-180 °C, IR (KBr, cm^{-1}): 1745 (β-lactam, C=O), ^{1}H-NMR ($CDCl_3$), δ (ppm): 3.86 (3H, s, OCH3), 6.02 (H_4, d, 1H, *J* = 5.15), 6.35 (H_3, d, 1H, *J* = 5.15), 6.56-7.44 (ArH, m, 18H), ^{13}C-NMR δ (ppm): 55.06 (OCH3), 84.12 (C3, β-lactam), 111.65-134.07 (aromatic carbons), 150.51 (C-OCH3), 156.99 (Ph-O-C_3), 164.93 (CO, β-lactam), MS (m/z, 75%): 445 (M), 446 (M+1), 324, 296, 134, 121, 107, 77, 69. Anal. Calcd for $C_{30}H_{23}NO_3$: C, 80.88; H, 5.20; N, 3.14 Found: C, 80.85; H, 5.19; N, 3.15.

4-(Anthracen-10-yl)-3-phenoxy-1-(pyrazin-2-yl) azetidin-2-one 3j

m.p: 100-102 °C, IR (KBr, cm^{-1}): 1760 (β-lactam, C=O), ^{1}H-NMR ($CDCl_3$), δ (ppm): 5.02 (H_4, d, *J* = 4.95), 5.76 (H_3, d, *J* = 4.95), 6.95-8.98 (ArH, m, 17H), ^{13}C-NMR δ (ppm): 61.5 (C4, β-lactam), 88.53 (C3, β-lactam), 114.66-135.26 (aromatic carbons), 143.23 (N-C), 156.01 (Ph-O-C_3), 163.09 (C=0), MS (m/z, 45%): 177, 121, 107, 93, 79, 77, 69. Anal. Calcd for $C_{27}H_{19}N_3O_2$: C, 77.68; H, 4.59; N, 10.07 Found: C, 77.62; H, 4.60; N, 10.03

4-(Naphthalen-yl)-3-phenoxy-1-(pyrazin-2-yl) azetidin-2-one 3k

m.p: 98-100 °C, IR (KBr, cm^{-1}): 1748 (β-lactam, C=O), ^{1}H-NMR ($CDCl_3$), δ (ppm): 5.26 (H_4, d, 1H, *J* = 5.73), 6.22 (H_3, d, 1H, *J* = 5.73), 6.61-7.95 (ArH, m, 15H), ^{13}C-NMR δ (ppm): 67.31 (C4, β-lactam), 87.02 (C3, β-lactam), 114.77-142.20 (aromatic carbons), 147.25 (N-C), 156.75 (Ph-O-C_3), 166.83 (C=0), MS (m/z, 100%): 246, 127, 121, 79, 77, 69. Anal. Calcd for $C_{23}H_{17}N_3O_2$: C, 75.19; H, 4.66; N, 11.44 Found: C, 75.13; H, 4.65; N, 11.40

4-(Anthracen-10-yl)-1-cyclohexyl-3-phenoxy-2-azetidinone 3l

m.p. 178-180 °C, IR (KBr, cm^{-1}): 1778.0 (β-lactam, C=O), ^{1}H-NMR δ (ppm): 0.88-2.11(m, 10H cyclohexyl protons), 3.50 (m, CH-N, cyclohexyl), 5.21(H_4, d, 1H, *J* = 1.55), 5.78 (H_3, d, 1H, *J* = 1.55), 6.53-7.97 (ArH, m, 14H), ^{13}C-NMR δ (ppm): 24.74-30.31 (cyclohexyl), 57.10 (CN, cyclohexyl), 115.37-129.89 (aromatic carbons), 157.73 (Ph-O-C_3), 167.23 (CO, β-lactam), MS (m/z, 70%): 422 (M+1), 421 (M), 328, 296, 239, 204, 134, 77, Anal. Calcd for $C_{29}H_{27}NO_2$: C, 82.63; H, 6.46; N, 3.32 Found: C, 82.60; H, 6.48; N, 3.29.

4-(Anthracen-10-yl)-1-cyclohexyl-3-methoxy-2-azetidinone 3m

m.p. 170-172 °C, IR (KBr, cm^{-1}): 1778.0 (β-lactam, C=O), ^{1}H-NMR δ (ppm): 0.88-1.71 (m, 10H cyclohexyl protons), 2.11 (m, CH-N, cyclohexyl),

3.50 (3H, s, CH_3)4.89 (H_4, d, 1H, *J* = 1.55), 5.78 (H_3, d, 1H, *J* = 1.55), 6.53-7.9 (ArH, m, 9H), ^{13}C-NMR δ (ppm): 24.74-30.31 (cyclohexyl), 57.10 (CN, cyclohexyl), 116.22-128.81 (aromatic carbons), 150.73 (CH_3-O-C_3), 167.25 (CO, β-lactam), MS (m/z, 50%): 359 (M), 328, 296, 239, 204, 134, 77, Anal. Calcd for $C_{24}H_{25}NO_2$: C, 80.19; H, 7.01; N, 3.90 Found: C, 80.16; H, 7.00; N, 3.95.

4-(Anthracen-10-yl)-1-(naphthalen-1-yl)-3-methoxyazetidin-2-one 3n

m.p: 233-235 °C, IR (KBr, cm^{-1}): 1763 (β-lactam, C=O), ^{1}H-NMR δ (ppm): 6.15 (H_4, d, 1H, *J* = 2.2), 6.55 (H_3, d, 1H, *J* = 2.2), 6.86-7.99 (ArH, m, 16H), ^{13}C-NMR δ (ppm): 61.75 (C4, β-lactam), 85.38 (C3, β-lactam), 115.73-131.46 (aromatic carbons), 144.00 (N-C), 157.50 (CH_3-O-C_3), 167.44 (CO, β-lactam), MS (m/z, 25%): 403(M), 331, 296, 177, 169, 134, 127, 77, 69, Anal. Calcd for $C_{28}H_{21}NO_2$: C, 83.35; H, 5.25; N, 3.47 Found: C, 83.31; H, 5.26; N, 3.44

4-(Anthracen-10-yl)-1-(4-methoxyphenyl)-3-methoxy-2- azetidinone 3o

IR (KBr, cm^{-1}): 1748 (β-lactam, C=O), ^{1}H-NMR δ (ppm): 3.30 (3H, s, OCH_3 β-lactam), 3.80 (3H, s, OCH_3), 5.42 (H_4, d, 1H, *J* = 1.5), 5.95 (H_3, d, 1H, *J* = 1.5), 6.76-7.90 (ArH, m, 16H), ^{13}C-NMR δ (ppm): 56.12 (CH_3), 57.11 (OCH_3, β-lactam), 58.23 (C4, β-lactam), 88.08 (C3, β-lactam), 114.75-138.46 (aromatic carbons), 157.50 (CH_3-O), 166.04 (CO, β-lactam). MS (m/z, 100%): 383 (M), 311, 276, 206, 177, 72, 69. Anal. Calcd for $C_{25}H_{21}NO_3$: C, 78.31; H, 5.52; N, 3.65 Found: C, 78.35; H, 5.50; N, 3.66

1-(4-Methoxyphenyl)-4-(naphthalene-2-yl)-3-phenoxy-1 azetidin-2-one 3p

m.p: 187-189 °C, IR (KBr, cm^{-1}): 1740 (β-lactam, C=O), ^{1}H-NMR δ (ppm): 3.78 (3H, s, OCH_3), 5.51 (H_4, d, 1H, *J* = 4.75), 5.62 (H_3, d, 1H, *J* = 5.00), 6.75-7.86 (16H, m, ArH), ^{13}C-NMR δ (ppm): 55.40 (OCH_3), 62.73 (C_4, β-lactam), 81.51 (C_3, β-lactam), 114.40-133.45 (aromatic carbons), 156.49 (Ph-O-C_3), 162.64 (C=O), Anal. Calcd for $C_{26}H_{21}NO_3$: C, 78.97; H, 5.35; N, 3.54 Found: C, 78.93; H, 5.35; N, 3.51.

3-Methoxy1-(4-methoxyphenyl)-4-(naphthalen-yl) azetidin-2-one 3q

m.p: 183-185 °C, IR (KBr, cm^{-1}): 1744 (β-lactam, C=O), ^{1}H-NMR δ (ppm): 3.17 (3H, s, OCH_3, β-lactam), 3.79 (3H, s, OCH_3), 4.88 (H_4, d, 1H, *J* = 1.25), 5.33 (H_3, d, 1H, *J* = 1.25), 6.71-7.86 (11H, m, ArH), ^{13}C-NMR δ (ppm): 55.40 (OCH_3), 58.53 (OCH_3, β-lactam), 62.09 (C_4, β-lactam), 85.06 (C_3, β-lactam), 114.35-133.48 (aromatic carbons), 156.36 (Ph-O-C_3), 167.11 (C=O), Anal. Calcd for $C_{21}H_{19}NO_3$: C, 75.66; H, 5.74; N, 4.20 Found: C, 75.67; H, 5.70; N, 4.25.

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