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A new insight into Beckmann rearrangement for the synthesis of some (*E*)-3-arylidenepiperidin-2-ones

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ABSTRACT

*Synthesis of some (E)-3-arylidenepiperidin-2-ones (**7**) derived from cyclopentanone (**1**) via thionyl chloride/dry dioxane mediated Beckmann rearrangement in moderate yields has been reported. The structural confirmation of the synthesized compounds was carried out on the basis of spectral (IR, NMR and mass) as well as elemental analysis results.*

Keywords: Beckmann rearrangement; (*E*)-2-arylidenecyclopentanones; oximes; (*E*)-3-arylidenepiperidin-2-ones.

INTRODUCTION

Piperidin-2-ones are *δ*-lactams which are considered to be one of the important classes of heterocycles due to profound applications associated with them. Piperidones act as intermediates in the synthesis of various glycosidase inhibitors [1,2], cyclic inhibitors of HIV protease [3], piperidine alkaloid (-)-adalinine [4], (±)-isoschizogamine alkaloid [5], *etc*. They are reported to possess immunostimulant and activation of Con A stimulated lymphocyte proliferation [6]. As a consequence, numberous methods have been developed in the past for their synthesis [7,8]. Beckmann rearrangement [9] has since long been known as an extremely useful and versatile method for the synthesis of amides from ketoximes. It provides a facile route for the incorporation of nitrogen into polycyclic structures for the synthesis of *N*-substuitued amides and lactams [10–17]. Moreover, this transformation also finds numerous applications in the synthesis of a variety of heterocyclic compounds [18–22] and aza steroids [23–29]. By far the most celebrated utility of Beckmann rearrangement to the mankind lies in the synthesis of caprolactam [11,30–34] which is being used daily in huge quantities all over the world for the manufacture of nylon 6. Despite wide intrest in the Beckmann rearrangement of a variety of saturated alicyclic, aliphatic and aromatic ketoximes, chemists in the recent past have exhibited only sporadic interest in Beckmann rearrangement of alicyclic [31,35–38] and cyclic *α*,*β*-unsaturated ketones [39–42]. A thorough literature survey revealed that Sato *et al* [38] carried out the Beckmann rearrangement of 2-benzylidenecyclopentanone *O*-tosyl oxime (**6**) in methanol-water (4:11) in the presence of piperidine (1%) under reflux, the major product obtained was 5-oxo-6-phenyl-1-hexanamide along with minor amount of (*E*)-6-benzylidenepiperidin-2-one (**9**), thereby proving that the rearrangement took place exclusively due to the migration of the arylidene group. Prompted by these observations coupled with a view to learn more about the Beckmann rearrangement of *α*,*β*-unsaturated ketones, we felt a need to reinvestigate the reaction. Herein, during the present investigation, Beckmann rearrangement of several (1*E*,2*E*)-2-arylidenecyclopentanone *O*-tosyl oximes (**6**) catalyzed by $SOCl_2$ in dry dioxane has been examined that resulted in the exclusive formation of (*E*)-3-arylidenepiperidin-2-ones (**7**) in moderate yields. Our main aim in the present investigation was to examine whether (i) (1*E*,2*E*)-2-arylidenecyclopentanone *O*-tosyl oximes (**6**) undrgo alkyl or vinyl migration and (ii) the rearrangement is accompanied by movement of the double bond from exocyclic to endocyclic position or not.

MATERIALS AND METHODS

The chemicals (AR and LR grade) used in the present investigation were purchased from Sigma-Aldrich, Qualigens, CDH, Himedia and Spectrochem. All the solvents were used as such or after necessary purification and dried according to the standard literature procedures. Melting points (°C) of various synthesized compounds were determined in open capillaries and are uncorrected. Purity of the synthesized compounds was checked by thin layer chromatography (TLC) using precoated silica gel (HF_{254}, 200 mesh) plates as stationary phase and various combinations of solvents as mobile phase. The visualization of the spots was carried out by using UV and iodine chamber. The progress of the reactions was also monitored by this method. The synthesis of compounds was done by stirring and/or heating. The synthesized compounds were characterized by employing different spectral (IR, NMR, Mass) and analytical techniques. The IR spectra of the synthesized compounds were scanned on Perkin Elmer Spectrum, BX II FTIR spectrometer in the range of 400^{-}4000 using potassium bromide (KBr) pellets and the values of wave numbers (υ) are reported in cm^{-1}. The ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Advance 300/400 MHz spectrometer at 300/400 MHz and 75/100 MHz, respectively in $CDCl_3$/DMSO-d_6. The chemical shifts are reported in parts per million (δ ppm) using tetramethylsilane (TMS) as an internal standard. The coupling constants (*J*) values are reported in Hertz (Hz). Mass spectra were recorded on Agilent 6310 LCMS ION TRAP spectrometer. The figure given in the parentheses represents relative intensity corresponding to the base peak taken as 100. Elemental analysis was carried out using Vario Micro Cube Elementar CHNS analyser. Analytical results for C, H and N were found within ±0.4% of the theoretical values.

4-Cyclopentenylmorpholine (2)

A mixture of cyclopentanone (42.0 g, 0.5 mole) and morpholine (52.2 g, 0.6 mole) in benzene (100 mL) was refluxed on a water bath under Dean and Stark apparatus for 10h until no further water collected. Therafter, the reaction mixture was distilled under vaccum to obtain 4-cyclopentenylmorpholine (**2**) in 70% yield, bp118–119°C/10 mm (Lit. [43] bp105–106°C/12 mm).

(*E*)-2-benzylidenecyclopentanone (4a)

A mixture of 4-cyclopentenylmorpholine (**2**, 7.65 g, 0.05 mole) and benzaldehyde (**3a**, 5.3 g, 0.05 mole) in benzene (100 mL) was refluxed on a water bath under Dean and Stark apparatus for 6h. Thereafter, the reaction mixture was cooled to room temperature and 50% HCl (30 mL) was added to it dropwise while stirring. Then, the reaction mixture was further stirred with the aid of a magnetic stirrer for 2h at room temperature, benzene layer was separated, washed with $NaHCO_3$ solution and then with water, dried over anhydrous $MgSO_4$ and benzene was distilled off to furnish a residue which upon crystallization from ethanol gave **(***E***)**-2-benzylidenecyclopentanone (**4a**) in 68% yield, mp 70–71°C (Lit. [44] mp 69–70°C; Lit. [43,45,46] mp 71–72°C).

Following exactly the same procedure as detailed in **4a,** the other (*E*)-2-arylidenecyclopentanones (**4b–4d**) were prepared from enamine (**2**) and the corresponding 4-substituted benzaldehydes (**3b–3d**). Their physical data are given in Table 1.

Table 1: Physical data of (*E*)-2-arylidenecyclopentanones (4)

Entry	R	Reaction conditions (xh+yh)^{a}	Yield (%)	mp (°C)	Lit.mp (°C	References
4a	H	6h+2h	68	70–71	69–72	43–46
4b	CH_3	7h+3h	65	60–62	62–65	44,47
4c	OCH_3	7h+2h	73.1	68	68–69	44,48
4d	Cl	7h+2h	70	75–78	77–80	44,49

^{a}*(xh+yh) indicates that initial refluxing for xh was followed by stirring for another yh at RT*

(1*E*,2*E*)-2-benzylidenecyclopentanone oxime (5a)

A mixture of (*E*)-2-benzylidenecyclopentanone (**4a**, 1.67 g, 0.009 mole), $NH_2OH.HCl$ (0.70 g, 0.01 mole) and NaOH (4.0 g) in methanol (150 mL) was refluxed on a water bath for 2h. Thereafter, the hot mixture was filtered and filtrate was concentrated *in vacuo*, water was added and the solid thus obtained was collected by filtration which upon crystallization from ethanol furnished (1*E*,2*E*)-2-benzylidenecyclopentanone oxime (**5a**) as yellow crystals in 79% yield, mp 127–129°C (Lit. [44] mp 127–129°C); IR (KBr, cm^{-1}): 3286 (br, O–H, stretch), 1631 (m, C=N, stretch), 1608 (s, C=C, stretch), 1485, 1290, 1220, 1184, 1101, 960, 827, 775, 727, 680, 503; ^{1}H NMR (300 MHz,

$CDCl_3$): δ 1.88 (*qn*, 2H, *J* = 7.5 Hz, H-4), 2.58 (*t*, 2H, *J* = 7.5 Hz, H-5), 2.83–2.92 (*m*, 2H, H-3), 6.98–7.38 (*m*, 6H, H-2′, H-3′, H-4′, H-5′, H-6′, H_β), 9.10 (*brs*, 1H, =N–OH, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.30 (C_4), 27.12 (C_5), 31.60 (C_3), 124.98, 127.54, 128.88, 129.64 ($C_{1'}$, $C_{2'}$, $C_{3'}$, $C_{4'}$, $C_{5'}$, $C_{6'}$), 136.12 (C_β), 137.39 (C_2), 163.88 (C_1); *Anal.* Calcd. for $C_{12}H_{13}NO$ (187.10): C, 76.98; H, 7.00; N, 7.48. Found: C, 76.81; H, 6.87; N, 7.73.

Following exactly the same procedure as detailed in **5a,** the other oximes (**5b–5d**) were prepared from the corresponding (*E*)-2-arylidenecyclopentanones (**4b–4d**). Their spectral parameters and other characteristics are given below:

(1*E*,2*E*)-2-(4-methylbenzylidene)cyclopentanone oxime (5b)

Obtained by refluxing for 2.5h as yellow crystals (ethanol), yield 72%, mp 136–138°C (Lit. [44] mp 132–134°C); IR (KBr, cm^{-1}): 3307 (br, O–H, stretch), 1622 (m, C=N, stretch), 1598 (s, C=C, stretch), 1478, 1305, 1256, 1168, 1115, 1005, 910, 868, 780, 723, 710, 625, 598, 503; ^1H NMR (300 MHz, DMSO-d_6): δ 1.86 (*qn*, 2H, *J* = 7.5 Hz, H-4), 2.36 (*s*, 3H, CH_3-4′), 2.62 (*t*, 2H, *J* = 7.5 Hz, H-5), 2.79–2.87 (*m*, 2H, H-3), 6.87 (*s*, 1H, H_β), 7.13 (*d*, 2H, *J* = 7.5 Hz, H-3′ & H-5′), 7.28 (*d*, 2H, *J* = 7.5 Hz, H-2′ & H-6′), 8.00–8.20 (*brs*, 1H, =N–OH, exchangeable with D_2O); ^{13}C NMR (75 MHz, DMSO-d_6): δ 21.40 ($C_{4'}$-CH_3), 22.85 (C_4), 27.36 (C_5), 31.89 (C_3), 124.23 ($C_{3'}$ & $C_{5'}$), 129.34 ($C_{2'}$ & $C_{6'}$), 129.88 ($C_{1'}$), 133.52 ($C_{4'}$), 135.02 (C_β), 137.55 (C_2), 163.13 (C_1); *Anal.* Calcd. for $C_{13}H_{15}NO$ (201.12): C, 77.58; H, 7.51; N, 6.96. Found: 77.32; H, 7.20; N, 6.72.

(1*E*,2*E*)-2-(4-methoxybenzylidene)cyclopentanone oxime (5c)

Obtained by refluxing for 2h as pale yellow crystals (methanol), yield 74%, mp 152–154°C (Lit. [44] mp 154–156°C); IR (KBr, cm^{-1}): 3257 (br, O–H, stretch), 1628 (m, C=N, stretch), 1589 (s, C=C, stretch), 1471, 1452, 1265, 1161, 1033, 937, 846, 746, 719, 696, 607, 547, 447; ^1H NMR (300 MHz, $CDCl_3$): δ 1.84 (*qn*, 2H, *J* = 7.5 Hz, H-4), 2.46 (*t*, 2H, *J* = 7.5 Hz, H-5), 2.75–2.83 (*m*, 2H, H-3), 3.80 (s, 3H, OCH_3-4′), 6.92 (*d*, 2H, *J* = 8.1 Hz, H-3′ & H-5′), 7.11 (*s*, 1H, H_β), 7.38 (*d*, 2H, *J* = 8.1 Hz, H-2′ & H-6′), 8.00–8.40 (*brs*, 1H, =N–OH, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.12 (C_4), 27.29 (C_5), 31.74 (C_3), 55.26 ($C_{4'}$-OCH_3), 113.82 ($C_{3'}$ & $C_{5'}$), 122.79 ($C_{2'}$ & $C_{6'}$), 129.88 ($C_{1'}$), 158.91 ($C_{4'}$), 132.69 (C_β), 134.17 (C_2), 163.22 (C_1); *Anal.* Calcd. for $C_{13}H_{15}NO_2$ (217.11): C, 71.87; H, 6.96; N, 6.45. Found: C, 71.63; H, 7.20; N, 6.70.

(1*E*,2*E*)-2-(4-chlorobenzylidene)cyclopentanone oxime (5d)

Obtained by refluxing for 2h as white crystals (methanol), yield 70%, mp 116–118°C (Lit. [44] mp 117–120°C); IR (KBr, cm^{-1}): 3250 (br, O–H, stretch), 1638 (m, C=N, stretch), 1611 (s, C=C, stretch), 1468, 1318, 1253, 1174, 1125, 1002, 945, 840, 727; ^1H NMR (300 MHz, $CDCl_3$): δ 1.92 (*qn*, 2H, *J* = 7.5 Hz, H-4), 2.53 (*t*, 2H, *J* = 7.5 Hz, H-5), 2.71–2.80 (*m*, 2H, H-3), 7.06 (*s*, 1H, H_β), 7.18–7.35 (*m*, 4H, H-2′, H-3′, H-5′, H-6′), 9.10 (*brs*, 1H, =N–OH, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.49 (C_4), 27.02 (C_5), 31.47 (C_3), 122.45 ($C_{3'}$ & $C_{5'}$), 128.86 ($C_{2'}$ & $C_{6'}$), 130.62 ($C_{1'}$), 133.51 ($C_{4'}$), 135.13 (C_β), 136.98 (C_2), 162.66 (C_1); *Anal.* Calcd. for $C_{12}H_{12}ClNO$ (221.06): C, 65.02; H, 5.46; N, 6.32. Found C, 65.30; H, 5.21; N, 6.61.

(1*E*,2*E*)-2-benzylidenecyclopentanone *O*-tosyl oxime (6a)

A solution of *p*-toluenesulphonyl chloride (1.90 g, 0.01 mole) in pyridine (7 mL) was added to a solution of (1*E*,2*E*)-2-benzylidenecyclopentanone oxime (1.87 g, 0.01 mole) in pyridine (7 mL) at 0°C and the reaction mixture was stirred with the aid of a magnetic stirrer for 2h at 0°C. Then reaction mixture was further stirred for 45 min at room temperature, and poured onto crushed ice containing 5 mL of dil. sulphuric acid. The solid thus obtained was collected by filteration and recrystallized from methanol to afford (1*E*,2*E*)-2-benzylidenecyclopentanone *O*-tosyl oxime (**6a**) as white crystals in 87% yield, mp 115–116°C (Lit. [38] mp 116–117°C); IR (KBr, cm^{-1}): 1598 (m, C=N, stretch), 1512, 1322, 1265, 1183, 1165, 840, 710, 553; ^1H NMR (300 MHz, $CDCl_3$): δ 1.90 (*qn*, 2H, *J* = 7.5 Hz, H-4), 2.39 (*s*, 3H, CH_3-4″), 2.69 (*t*, 2H, *J* = 7.5 Hz, H-5), 2.71–2.79 (*m*, 2H, H-3), 6.88–7.58 (*m*, 8H, H-2′, H-3′, H-4′, H-5′, H-6′, H-3″, H-5″, H_β), 7.91 (*d*, 2H, *J* = 8.4 Hz, H-2″ & H-6″); ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.96 ($C_{4''}$-CH_3), 21.30, 26.75, 29.81 (C_3, C_4, C_5), 123.18, 127.45, 127.90, 128.60, 129.52, 130.74, 131.22, ($C_{1'}$, $C_{2'}$, $C_{3'}$, $C_{4'}$, $C_{5'}$, $C_{6'}$, $C_{2''}$, $C_{3''}$, $C_{4''}$, $C_{5''}$, $C_{6''}$), 136.70 (C_β), 137.63 (C_2), 143.32 ($C_{1''}$), 162.55 (C_1); *Anal.* Calcd. for $C_{19}H_{19}NO_3S$ (341.11): C, 66.84; H, 5.61; N, 4.10. Found: C, 66.54; H, 5.82; N, 4.33.

Following exactly the same procedure as detailed in **6a,** the other *O*-tosyl oximes (**6b–6d**) were prepared from the corresponding oximes (**5b–5d**). Their spectral parameters and other characteristics are given below:

(1*E*,2*E*)-2-(4-methylbenzylidene)cyclopentanone *O*-tosyl oxime (**6b**)
Obtained by stirring for 3h as yellowish white crystals (methanol), yield 81%, mp 123–124°C; IR (KBr, cm^{-1}): 1586 (m, C=N, stretch), 1501, 1368, 1214, 1196, 1132, 1056, 822, 756, 510; ^{1}H NMR (300 MHz, CDCl$_3$): δ 1.88 (*qn*, 2H, *J* = 7.5 Hz, H-4), 2.37 (*s*, 3H, CH$_3$-4′), 2.39 (*s*, 3H, CH$_3$-4″), 2.68 (*t*, 2H, *J* = 7.5 Hz, H-5), 2.82–2.90 (*m*, 2H, H-3), 6.89 (*s*, 1H, H$_\beta$), 7.17 (*d*, 2H, *J* = 7.5 Hz, H-3′ & H-5′), 7.30 (*d*, 2H, *J* = 7.5 Hz, H-2′ & H-6′), 7.42 (*d*, 2H, *J* = 8.4 Hz, H-3″ & H-5″), 7.89 (*d*, 2H, *J* = 8.4 Hz, H-2″ & H-6″); ^{13}C NMR (75 MHz, CDCl$_3$): δ 20.13 (C$_{4''}$-*CH$_3$*), 21.26 (C$_{4'}$-*CH$_3$*), 21.52, 26.57, 29.71 (C$_3$, C$_4$, C$_5$), 125.25, 127.45, 127.92, 129.15, 130.80, 133.15, 133.75, (C$_{1'}$, C$_{2'}$, C$_{3'}$, C$_{4'}$, C$_{5'}$, C$_{6'}$, C$_{2''}$, C$_{3''}$, C$_{4''}$, C$_{5''}$, C$_{6''}$), 136.54 (C$_\beta$), 138.17 (C$_2$), 143.34 (C$_{1''}$), 161.22 (C$_1$); *Anal.* Calcd. for C$_{20}$H$_{21}$NO$_3$S (355.12): C, 67.58; H, 5.95; N, 3.94. Found C, 67.86; H, 6.23; N, 3.62.

(1*E*,2*E*)-2-(4-methoxybenzylidene)cyclopentanone *O*-tosyl oxime (**6c**)
Obtained by stirring for 2h as white crystals (methanol), yield 88.3%, mp 140–142°C; IR (KBr, cm^{-1}): 1595 (m, C=N, stretch), 1496, 1328, 1304, 1183, 1094, 1024, 865, 722, 503; ^{1}H NMR (300 MHz, CDCl$_3$): δ 1.80 (*qn*, 2H, *J* = 7.5 Hz, H-4), 2.40 (s, 3H, CH$_3$-4″), 2.64 (*t*, 2H, *J* = 7.5 Hz, H-5), 2.81–2.88 (*s*, 2H, H-3), 3.82 (*s*, 3H, OCH$_3$-4′), 6.95 (*d*, 2H, *J* = 8.1 Hz, H-3′ & H-5′), 7.08 (*s*, 1H, H$_\beta$), 7.35–7.49 (*m*, 4H, H-2′, H-6′, H-3″, H-5″), 7.85 (*d*, 2H, *J* = 8.4 Hz, H-2″ & H-6″); ^{13}C NMR (75 MHz, CDCl$_3$): δ 20.34 (C$_{4''}$-*CH$_3$*), 21.16, 26.92, 30.32 (C$_3$, C$_4$, C$_5$), 55.26 (C$_{4'}$-*OCH$_3$*), 113.50 (C$_{3'}$ & C$_{5'}$), 122.32, 127.52, 127.96, 129.50, 131.20 (C$_{1'}$, C$_{2'}$, C$_{4'}$, C$_{6'}$, C$_{2''}$, C$_{3''}$, C$_{4''}$, C$_{5''}$, C$_{6''}$), 134.50 (C$_\beta$), 136.88 (C$_2$), 143.31 (C$_{1''}$), 159.02 (C$_{4'}$), 160.98 (C$_1$); *Anal.* Calcd. for C$_{20}$H$_{21}$NO$_4$S (371.12): C, 64.67; H, 5.70; N, 3.77. Found: C, 64.90; H, 5.43; N, 4.03.

(1*E*,2*E*)-2-(4-chlorobenzylidene)cyclopentanone *O*-tosyl oxime (**6d**)
Obtained by stirring for 2h as white crystals (methanol), yield 81.2%, mp 167–169°C; IR (KBr, cm^{-1}): 1602 (m, C=N, stretch), 1535, 1335, 1284, 1150, 954, 813, 756, 535; ^{1}H NMR (400 MHz, CDCl$_3$): δ 1.86 (*qn*, 2H, *J* = 7.5 Hz, H-4), 2.38 (*s*, 3H, CH$_3$-4″), 2.72 (*t*, 2H, *J* = 7.5 Hz, H-5), 2.85–2.96 (*m*, 2H, H-3), 7.13 (*s*, 1H, H$_\beta$), 7.22–7.46 (*m*, 6H, H-2′, H-3′, H-5′, H-6′, H-3″, H-5″), 7.92 (*d*, 2H, *J* = 8.4 Hz, H-2″ & H-6″); ^{13}C NMR (100 MHz, CDCl$_3$): δ 20.81 (C$_{4''}$-*CH$_3$*), 21.50, 26.88, 30.52 (C$_3$, C$_4$, C$_5$), 122.23, 127.40, 127.95, 129.45, 130.72, 131.31, 134.12 (C$_{1'}$, C$_{2'}$, C$_{3'}$, C$_{4'}$, C$_{5'}$, C$_{6'}$, C$_{2''}$, C$_{3''}$, C$_{4''}$, C$_{5''}$, C$_{6''}$), 135.01 (C$_\beta$), 136.22 (C$_2$), 143.20 (C$_{1''}$), 161.66 (C$_1$); *Anal.* Calcd. for C$_{19}$H$_{18}$ClNO$_3$S (375.07): C, 60.71; H, 4.83; N, 3.73. Found C, 60.95; H, 4.52; N, 3.41.

(*E*)-3-benzylidenepiperidin-2-one (7a)
A solution of (1*E*,2*E*)-2-benzylidenecyclopentanone *O*-tosyl oxime (**6a**, 0.500 g, 0.00146 mole) and SOCl$_2$ (0.521 mL) in dry dioxane (30 mL) was stirred with the aid of a magnetic stirrer at room temperature for 10h. Thereafter, water was added to the reaction mixture and it was extracted with diethyl ether (3×20 mL). The combined extracts were washed with water, NaHCO$_3$, and water and dried over anhydrous Na$_2$SO$_4$. Rotaevaporation of the solvent furnished a solid which upon crystallization from benzene furnished (*E*)-3-benzylidenepiperidin-2-one (**7a**) as light brown crystals, yield 45%, mp 126–128°C (Lit. [50] mp 152–154°C; (Lit. [51] mp 155–156°C); IR (KBr, cm^{-1}): 3268 (m, N–H, stretch), 1656 (m, C=O, stretch), 1630 (s, C=C, stretch), 1470, 1410, 1341, 1105, 903, 845; ^{1}H NMR (300 MHz, CDCl$_3$): δ 1.92–1.98 (*m*, 2H, H-5), 2.80–2.91 (*m*, 2H, H-4), 3.43–3.50 (*m*, 2H, H-6), 6.34 (*brs*, 1H, N-H, exchangeable with D$_2$O), 7.26–7.39 (*m*, 5H, H-2′, H-3′, H-4′, H-5′, H-6′), 7.81 (*s*, 1H, H$_\beta$); ^{13}C NMR (75 MHz, CDCl$_3$): δ 23.46 (C$_5$), 29.17 (C$_4$), 42.30 (C$_6$), 128.65, 129.60, 130.23, 131.45 (C$_{1'}$, C$_{2'}$, C$_{3'}$, C$_{4'}$, C$_{5'}$, C$_{6'}$), 133.62 (C$_\beta$), 137.41 (C$_3$), 166.23 (C$_2$); ESI-MS m/z: 187 (M$^{+\cdot}$, 52), 186 (100), 159 (7.2), 130 (6.8), 129 (12.8), 116 (4.5), 115 (18), 102 (9.2), 91 (7.8), 77 (5.2); *Anal.* Calcd. for C$_{12}$H$_{13}$NO (187.10): C, 76.98; H, 7.00; N, 7.48. Found: C, 76.73; H, 7.26; N, 7.85.

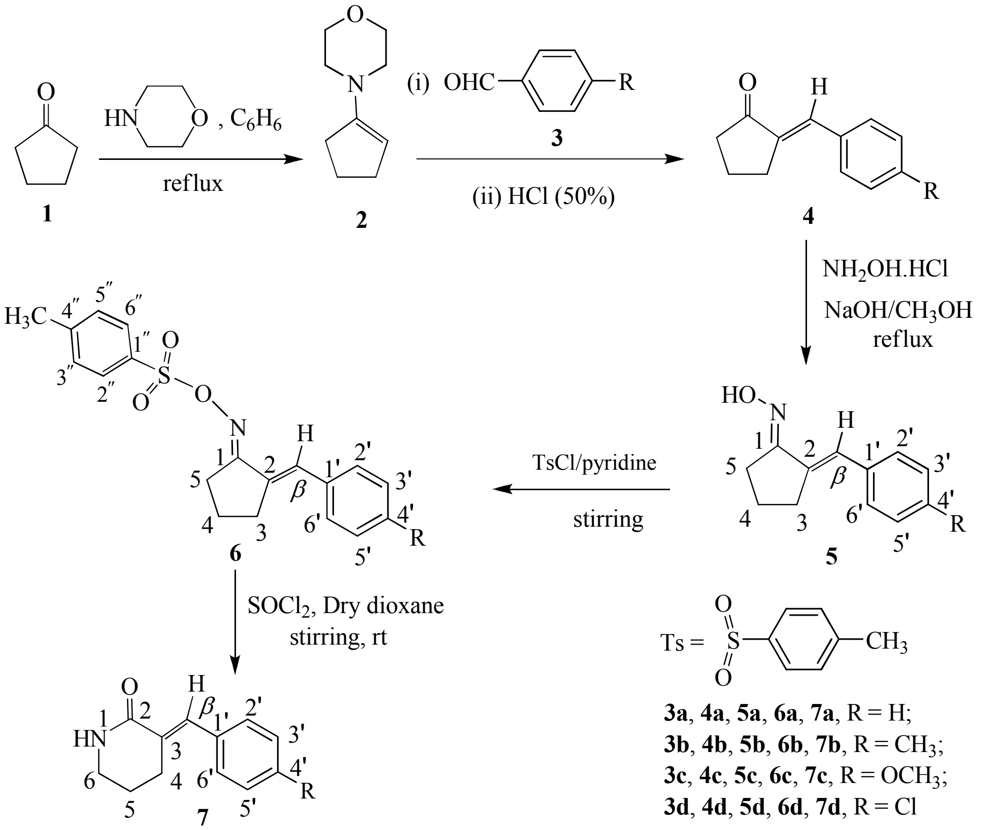
Following exactly the same procedure as detailed in **7a,** the other (*E*)-3-arylidenepiperidin-2-one**s** (**7b–7d**) were prepared from the corresponding *O*-tosyl oximes (**6b–6d**). Their spectral parameters and other characteristics are given below:

(*E*)-3-(4-methylbenzylidene)piperidin-2-one (**7b**)
Obtained by stirring for 11h as white crystals (methanol), yield 42%, mp 125–127°C (Lit. [50] mp 182–184°C; Lit. [51] mp 183–184°C); IR (KBr, cm^{-1}): 3290 (m, N–H, stretch), 1680 (s, C=O, stretch), 1614 (s, C=C, stretch), 1456, 1398, 1330, 1210, 1017, 824, 701; ^{1}H NMR (300 MHz, CDCl$_3$): δ 1.89–1.93 (*m*, 2H, H-5), 2.36 (*s*, 3H, CH$_3$-4′), 2.78–2.94 (*m*, 2H, H-4), 3.42–3.47 (*m*, 2H, H-6), 6.12 (*brs*, 1H, N-H, exchangeable with D$_2$O), 7.20 (*d*, 2H, *J* = 7.5 Hz, H-3′ & H-5′), 7.32 (*d*, 2H, *J* = 7.5 Hz, H-2′ & H-6′), 7.85 (*s*, 1H, H$_\beta$); ^{13}C NMR (75 MHz, CDCl$_3$): δ 21.30 (C$_{4'}$-*CH$_3$*), 23.70 (C$_5$), 29.47 (C$_4$), 42.06 (C$_6$), 129.23, 129.75, 130.78, 133.45 (C$_{1'}$, C$_{2'}$, C$_{3'}$, C$_{4'}$, C$_{5'}$, C$_{6'}$), 134.72 (C$_\beta$), 137.85 (C$_3$), 167.04 (C$_2$); ESI-MS m/z: 201 (M$^{+\cdot}$, 50.8), 200 (100), 186 (5.1), 173 (6.8), 172 (4.4), 143 (7.4), 130

(3.8), 129 (14.3), 128 (10.8), 116 (4.8), 115 (16.2), 105 (3.8), 91 (0.8), 77 (0.9); *Anal.* Calcd. for $C_{13}H_{15}NO$ (201.12): C, 77.58; H, 7.51; N, 6.96. Found: C, 77.26; H, 7.80; N, 6.62.

(*E*)-3-(4-methoxybenzylidene)piperidin-2-one (7c)
Obtained by stirring for 10h as brown crystals (ethanol), yield 45%, mp 164–166°C (Lit. [50] mp 205–207°C; Lit. [51] mp 210–211°C); IR (KBr, cm^{-1}): 3177 (m, N–H, stretch), 1677 (s, C=O, stretch), 1605 (s, C=C, stretch), 1488, 1404, 1325, 1168, 960, 922, 760; ^1H NMR (400 MHz, $CDCl_3$): δ 1.84–1.90 (*m*, 2H, H-5), 2.83–2.92 (*m*, 2H, H-4), 3.43–3.49 (*m*, 2H, H-6), 3.82 (*s*, 3H, OCH_3-4′), 5.82 (*brs*, 1H, N-H, exchangeable with D_2O), 6.98 (*d*, 2H, *J* = 8.4 Hz, H-3′ & H-5′), 7.40 (*d*, 2H, *J* = 8.4 Hz, H-2′ & H-6′), 7.78 (*s*, 1H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.86 (C_5), 29.01(C_4), 42.61 (C_6), 55.30 ($C_{4'}$-OCH_3), 113.56 ($C_{3'}$ & $C_{5'}$), 129.91, 131.39 ($C_{1'}$, $C_{2'}$ & $C_{6'}$), 133.68 (C_β), 136.23 (C_3), 159.35 ($C_{4'}$), 162.42 (C_2); ESI-MS m/z: 217 ($M^{+\cdot}$, 72.3), 216 (100), 202 (5.5), 189 (7.2), 174 (18.3), 160 (4.8), 159 (8.1), 145 (7.2), 121 (7.1), 115 (14.6), 91 (5.2); *Anal.* Calcd. for $C_{13}H_{15}NO_2$ (217.11): C, 71.87; H, 6.96; N, 6.45. Found: C, 71.58; H, 6.68; N, 6.77.

(*E*)-3-(4-chlorobenzylidene)piperidin-2-one (7d)
Obtained by stirring for 12h as pale yellow crystals (methanol), yield 40%, mp 165–168°C (Lit. [51] mp 79–81°C); IR (KBr, cm^{-1}): 3217 (m, N–H, stretch), 1662 (s, C=O, stretch), 1640 (s, C=C, stretch), 1474, 1420, 1328, 1193, 1105, 914, 741; ^1H NMR (300 MHz, $CDCl_3$): δ 1.90–1.95 (*m*, 2H, H-5), 2.85–2.96 (*m*, 2H, H-4), 3.41–3.46 (*m*, 2H, H-6), 5.64 (*brs*, 1H, N-H, exchangeable with D_2O), 7.28 (*d*, 2H, *J* = 8.1 Hz, H-3′ & H-5′), 7.42 (*d*, 2H, *J* = 8.1 Hz, H-2′ & H-6′), 7.90 (*s*, 1H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.16 (C_5), 29.69 (C_4), 42.38 (C_6), 122.65, 129.53, 130.92, 132.73 ($C_{1'}$, $C_{2'}$, $C_{3'}$, $C_{4'}$, $C_{5'}$, $C_{6'}$), 135.23 (C_β), 137.12 (C_3), 165.75 (C_2); ESI-MS m/z: 221 ($M^{+\cdot}$, 55.3)/223 ($M^{+\cdot}$+2, 17.6), 220 (100)/222 (35.2), 193 (14.4)/195 (4.9), 186 (24), 158 (2.3), 125 (5.7)/127 (1.8), 115 (16.4); *Anal.* Calcd. for $C_{12}H_{12}ClNO$ (221.06): C, 65.02; H, 5.46; N, 6.32. Found: C, 65.33; H, 5.30; N, 6.65.



3a, **4a**, **5a**, **6a**, **7a**, R = H;
3b, **4b**, **5b**, **6b**, **7b**, R = CH_3;
3c, **4c**, **5c**, **6c**, **7c**, R = OCH_3;
3d, **4d**, **5d**, **6d**, **7d**, R = Cl

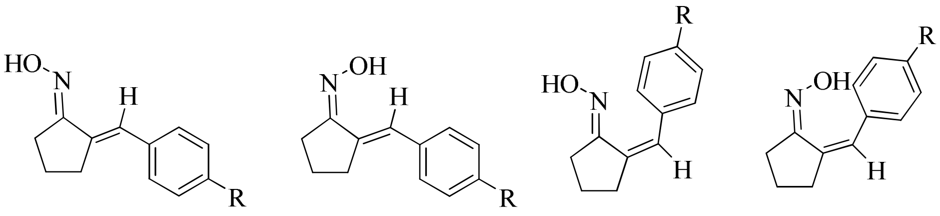
Scheme 1: Synthetic route of (*E*)-3-arylidenepiperidin-2-ones (7)

RESULTS AND DISCUSSION

The general approach towards the synthesis of (*E*)-3-arylidenepiperidin-2-ones (**7**) derived from cyclopentanone (**2**) is outlined in Scheme 1. The synthesis of (*E*)-2-arylidenecyclopentanones (**4a–4d**) was accomplished by the method used by Birkofer *et al* [43] which involves firstly reacting the cyclopentanone (**1**) with morpholine to produce 4-cyclopentenylmorpholine (**2**). Thereafter, the condensation of **2** was carried out with appropriate 4-substituted benzaldehydes (**3**) followed by cleaving the products under acidic conditions to furnish the corresponding (*E*)-2-arylidenecyclopentanones (**4a–4d**) in good yields (68–73.1%). The purity of the entire synthesized (*E*)-2-arylidenecyclopentanones (**4a–4d**) was checked through TLC and melting points.

The synthesis of oximes (**5a–5d**) was carried out by refluxing a mixture of an appropriate (*E*)-2-arylidenecyclopentanone (**4**, 0.09 mole), $NH_2OH.HCl$ (7.0 g, 0.1 mole) and NaOH (4.0 g) in methanol (150 mL) for 2–2.5h. The usual work up of the resulting reaction mixture furnished a solid which upon crystallization from ethanol afforded the corresponding (1*E*,2*E*)-2-arylidenecyclopentanone oximes (**5a–5d**) in high yields (70–79%).

The structures of all the oximes thus synthesized were established on the basis of IR, ^{1}H NMR and ^{13}C NMR spectral analysis. In principle, the oximes (**5a–5d**) can exist in four stereoisomeric forms on the basis of differences in orientation around C=N and C=C bonds, *i.e.* (1*E*,2*E*)-**5a–5d**, (1*Z*,2*E*)-**5a–5d**, (1*E*,2*Z*)-**5a–5d** and (1*Z*,2*Z*)-**5a–5d** (Fig. 1)



(1*E*,2*E*)-**5a–5d** (1*Z*,2*E*)-**5a–5d** (1*E*,2*Z*)-**5a–5d** (1*Z*,2*Z*)-**5a–5d**

R = H, CH_3, OCH_3, Cl

Fig.1: Different orientations of 5 around C=N and C=C bonds

Out of the four possible stereoisomeric forms, the configurations, (1*Z*,2*Z*) and (1*E*,2*Z*) for the oximes (**5a–5d**) can easily be discarded on the basis of arguments presented above:

Since the precursor ketones (**4a–4d**) possess (*E*)-configuration and it is highly unlikely that under base-catalyzed equilibrium conditions, a thermodynamically more stable ketone with (*E*)-configuration is converted into a thermodynamically less stable ketone with (*Z*)-configuration, therefore, it seems logical to assume that during the formation of oximes (**5**), there is no change in configuration around C=C, hence the configurations (1*Z*,2*Z*) and (1*E*,2*Z*) for the oximes (**5**) stand rejected.

In order to distinguish between the remaining two configurations, *i.e.* (1*E*,2*E*) and (1*Z*,2*E*), their IR, ^{1}H NMR and ^{13}C NMR spectra were critically examined. The IR spectra of all the oximes (**5a–5d**), in each case, exhibited a broad absorption band of medium intensity in the region at 3250–3307 cm^{-1} due to O–H stretching, a band of weak intensity in the region at 1622–1638 cm^{-1} due to C=N stretching and another band of medium intensity in the region at 1589–1611 cm^{-1} due to C=C stretching. The ^{1}H NMR (300 MHz, $CDCl_3$/DMSO-d_6) spectra of oximes (**5a–5d**), displayed the required integral ratio of aromatic to non-aromatic protons. The oximes (**5a–5d**), in the aliphatic region, exhibited a quintet (J = 7.5 Hz) integrating for two protons in the region at δ 1.84–1.92 which can safely be assigned to C_4-protons. Next, towards the lower field, was located a two-proton triplet in the region at δ 2.46–2.62 (J = 7.5 Hz) due to C_5-protons followed by a two-proton multiplet exhibited in the region at δ 2.71–2.92 assignable to C_3-protons. The vinylic proton (C_β-H) in the oximes (**5b–5d**) was displayed as a singlet in the region at δ 6.87–7.11. However, in **5a**, the vinylic proton and aromatic protons were observed as a complex multiplet in the region at δ 6.98–7.38. The signal due to the proton of oxime (=N–OH) group, in each case, was observed as a broad singlet (exchangeable with D_2O) in the region at δ 8.00–9.10. The signals due to the remaining aliphatic and aromatic protons were observed in the expected regions (*vide experimental*). The ^{13}C NMR spectra of oximes (**5a–5d**), in the aliphatic region, in each case, exhibited signals due to three methylene carbons in the regions at δ 22.12–22.85, δ

27.02–27.36 and δ 31.47–31.89. The signal observed in the region at δ 22.12–22.85 can reasonably be assigned to C_4 as it is located away from the conjugated part. The signal exhibited in the region at δ 27.02–27.36 was safely assigned to C_5. The signal displayed in the region at δ 31.47–31.89 was undoubtedly assigned to C_3. The signals due to vinylic carbon atoms (C_β and C_2) were observed in the regions at δ 132.69–136.12 and δ 134.17–137.55, respectively. The signal exhibited in the most downfield region at δ 162.66–163.88 was safely assigned to C_1. The signals due to the remaining aliphatic and aromatic carbons were observed in the expected regions (*vide experimental*). All these assignments are in accord with the results reported in the literature by Hawkes *et al* [52] and Austin *et* al [44] who revealed that the chemical shifts of oximino *α*-methylene carbons depend upon their orientation relative to the oximino oxygen and reported that the resonance for *syn* configuration was found at a lower chemical shift value than for the *anti* arrangement. Hence, on the basis of chemical shift values (δ 27.02–27.36) of C_5 in ^{13}C NMR spectra of oximes (**5a–5d**), the configuration around C=N and C=C bonds is reasonably assumed as (1*E*,2*E*).

The *O*-tosyl oximes (**6a–6d**) needed for the purpose were prepared by stirring a solution of an appropriate oxime (**5a–5d**, 0.01 mole) and *p*-toluenesulphonyl chloride (1.90 g, 0.01 mole) in pyridine at room temperature for 2–3h in excellent yields (81–88.3%).

Since during the tosylation of oximes (**5a–5d**), the C=C and C=N bonds are not affected, hence it is reasonable to assume that the configuration of oximes, *i.e.* (1*E*,2*E*) is retained in their *O*-tosyl oximes (**6a–6d**).

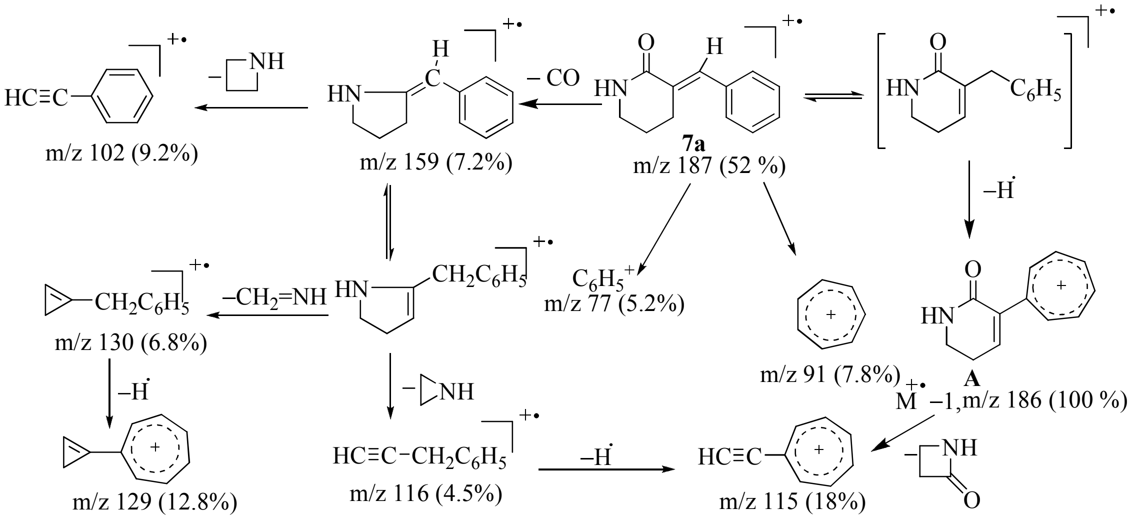
The structures of all the *O*-tosyl oximes (**6a–6d**) have been established on the basis of their spectral (IR, ^{1}H NMR and ^{13}C NMR) as well as analytical results. The IR spectra of *O*-tosyl oximes (**6a–6d**) displayed the characteristic absorption due to C=N stretching in the region at 1586–1602 cm^{-1}. The ^{1}H NMR (300/400 MHz, $CDCl_3$) spectra of *O*-tosyl oximes (**6a–6d**), in each case, displayed the required integral ratio of aromatic to non-aromatic protons. The C_4-protons in **6a–6d** were observed as a two-proton quintet in the region at δ 1.80–1.90. Next, towards the lower field was located a three-proton singlet in the region at δ 2.38–2.40 corresponding to the methyl protons located at $C_{4'''}$ followed by a two-proton triplet (*J* = 7.5 Hz) in the region at δ 2.64–2.72 due to C_5-protons and another two-proton multiplet in the region at δ 2.71–2.96 assignable to C_3-protons. The signal displayed in the region at δ 6.88–7.13 was safely assigned to vinylic proton (C_β-H). At the lowest field of the spectra, in each case, was located a two-proton doublet (*J* = 8.4 Hz) in the region at δ 7.85–7.92 assignable to $C_{2'''}$-H and $C_{6'''}$-H which finds support from the results reported in the literature [38,53]. The signals due to the remaining aliphatic and aromatic protons were observed in the expected regions (*vide experimental*). The ^{13}C NMR spectra of *O*-tosyl oximes (**6a–6d**), in each case, in the aliphatic region at highest field, displayed a signal at δ 20.13–20.96 due to methyl carbon present at $C_{4''}$. Next, towards the lower field were observed signals in the aliphatic regions at δ 21.16–21.52, δ 26.57–26.92 and δ 29.71–30.52 due to the methylene carbons (C_3, C_4, C_5). The signals displayed in the regions at δ 134.50–136.70 and δ 136.22–138.17 were assigned to C_β and C_2, respectively. The signal due to $C_{1''}$, characteristic of tosyl group, was appeared in the region at δ 143.20–144.34. The signal exhibited in the most downfield region at δ 160.98–162.55 was safely assigned to C_1. The remaining aliphatic and aromatic carbons were found to display signals in their characteristic regions (*vide experimental*).

The (*E*)-3-arylidenepiperidin-2-ones (**7**) were prepared from the corresponding (1*E*,2*E*)-2-arylidenecyclopentanone *O*-tosyl oximes (**6**) by $SOCl_2$ catalyzed Beckmann rearrangement in dry dioxane under stirring at room temperature for 10–12h in moderate yields (40–45%).

Firstly, a solution of (1*E*,2*E*)-2-benzylidenecyclopentanone *O*-tosyl oxime (**6a**, 0.500 g, 0.00146 mole) in dry dioxane (30 mL) was subjected to Beckmann rearrangement by stirring with $SOCl_2$ (0.521 mL) at room temperature for 10h. Usual work up of the reaction mixture furnished a residue which upon crystallization from benzene furnished (*E*)-3-benzylidenepiperidin-2-one (**7a**) in 45% yield. The TLC analysis of the mother liquor left after filtration of the lactam (**7a**) revealed the presence of starting *O*-tosyl oxime (**6a**) along with traces of the lactam (**7a**) thereby confirming that Beckmann rearrangement of (1*E*,2*E*)-2-benzylidenecyclopentanone *O*-tosyl oxime (**6a**) furnished (*E*)-3-benzylidenepiperidin-2-one (**7a**) as a single product.

The structure of (*E*)-3-benzylidenepiperidin-2-one (**7a**) has been established on the basis of spectral (IR, ^{1}H NMR, ^{13}C NMR and mass) as well as analytical results. The IR spectrum of **7a** exhibited a medium intensity absorption band at 3268 cm^{-1} due to N–H stretching of secondary amide. Also there were present two strong absorption bands in the functional group regions at 1656 cm^{-1} and 1630 cm^{-1} assignable to C=O stretching of *α*,*β*-unsaturated amide group and C=C stretching, respectively. The ^{1}H NMR (300 MHz, $CDCl_3$) spectrum, in the aliphatic region, at the highest field, displayed a mutiplet in the region at δ 1.92–1.98 integrating for two protons which could safely be assigned to C_5-methylene protons. It was followed by another two-proton multiplet exhibited in the region at δ 2.80–2.91 ascribable to C_4-methylene protons. The deshielding of C_4-protons relative to C_5-protons is presumably due to C=C bond adjacent to C_4. A two-proton multiplet observed in the region at δ 3.43–3.50 was assigned to C_6-methylene protons. Another distinguishing feature of ^{1}H NMR spectrum of **7a** was the presence of a sharp singlet at δ 7.81 which can safely be assigned to C_β-H. The downfield shifting of C_β-H can be attributed to the reason that it lies in the deshielding zone of C=O group. The five aromatic protons of the phenyl group ($C_{2'}$-H, $C_{3'}$-H, $C_{4'}$-H, $C_{5'}$-H, $C_{6'}$-H), however, appeared as a complex multiplet in the region at δ 7.26–7.39. The N-H proton was observed as a broad singlet (exchangeable with D_2O) at δ 6.34. The ^{13}C NMR spectrum of **7a** in the aliphatic region exhibited a signal at δ 23.46. The most suitable contender for this signal seems to be C_5. Next, towards the lower field, was located a signal at δ 29.17 assignable to C_4. The signal observed at δ 42.30 was assigned to C_6. The signals observed at δ 128.65, δ 129.60, δ 130.23 and δ 131.45 were assigned to the carbon atoms of phenyl ring ($C_{1'}$, $C_{2'}$, $C_{3'}$, $C_{4'}$, $C_{5'}$, $C_{6'}$). The signals displayed at δ 133.62 and δ 137.41 were assigned to vinylic carbons, *i.e.* C_β and C_3, respectively. At the lowest field of the spectrum, was exhibited a signal at δ 166.23, which was safely assigned to C_2, *i.e* carbon of C=O group. The structure of the lactam (**7a**) was further corroborated by its mass fragmentation that exhibited the molecular ion peak of moderate abundance at m/z 187 (52%). The loss of H atom from the molecular ion furnished an ion peak at m/z 186 (100%) which forms the base peak. Although a number of structures can be envisioned for this $M^{+\cdot}$–1 ion, yet tropylium ion (**A**) seems to be the most stable structure as shown in Scheme 2. The formation of tropylium ion (**A**) has presumably occurred through an initial migration of exocyclic double bond to endocyclic position followed by loss of an H-atom. The sequential loss of CO and aziridine moiety from the molecular ion furnished ion peaks at m/z 159 (7.2%) and m/z 116 (4.5%), respectively. The ion peak at m/z 116 upon further loss of H-atom constituted another ion peak at m/z 115 (18%). The similar ion peak at m/z 115 may also arise by elision of azetidinone moiety from **A**. Moreover, direct loss of azetidine from the ion peak at m/z 159 furnished another peak of low intensity at m/z 102 (9.2%). Alternatively, the ion peak at m/z 159 may sequentially eliminate CH_2=NH and H-atom, respectively to give ion peaks at m/z 130 (6.8%) and 129 (12.8%). Lastly, the obtention of ion peaks at m/z 77 (5.2%) and m/z 91 (7.8%) due to phenyl cation and tropylium cation, respectively supports the presence of benzylidene moiety in the lactam (**7a**). The genesis of some of these peaks is sketched in Scheme 2.

Further, the analytical results of **7a** were found in consistent with its molecular formula. *Anal.* Calcd. for $C_{12}H_{13}NO$ (187.10): C, 77.58%; H, 7.51%; N, 6.96 %. Found: C, 77.76%; H, 7.84%; N, 7.21%.

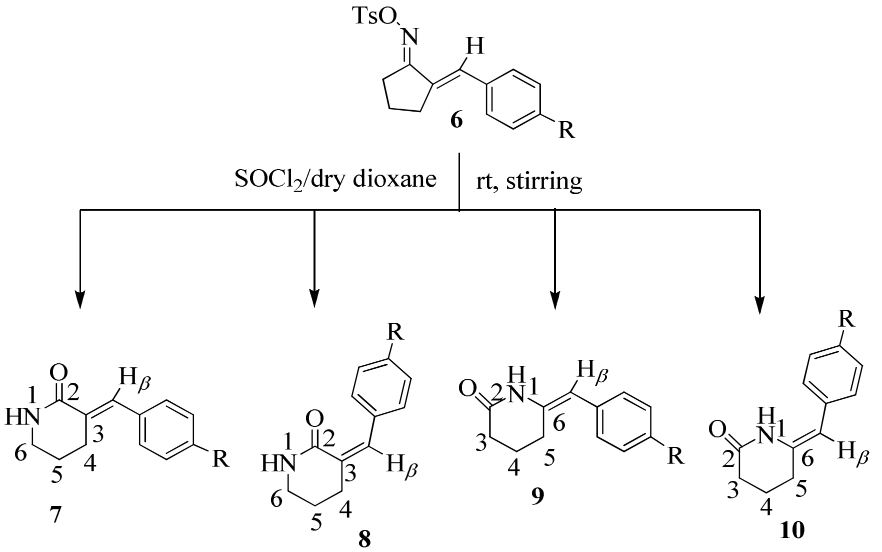


Scheme 2: Mas fragmentation pattern of 7a

Subsequently, to establish the generality of the reaction, the thionyl chloride mediated Beckmann rearrangement of (1*E*,2*E*)-2-arylidenecyclopentanone *O*-tosyl oximes (**7b–7d**) was carried out under similar reaction conditions as employed for **7a.** Here again, the usual work up of the reaction mixture yielded the corresponding (*E*)-3-arylidenepiperidin-2-ones (**7b–7d**) in 42–45% yields. Like (*E*)-3-benzylidenepiperidin-2-one (**7a**), the structures of all the lactams (**7b–7d**) have been confirmed on the basis of their spectral (IR, ^{1}H NMR, ^{13}C NMR and mass) as well as analytical results.

The IR spectra of (**7b–7d**) displayed characteristic medium intensity absorption bands in the region at 3177–3290 cm^{-1} due to N–H stretching of secondary amide. The two strong absorption bands due to C=O stretching of amide group and C=C stretching were observed in the regions at 1662–1680 cm^{-1} and 1614–1640 cm^{-1}, respectively. The ^{1}H NMR spectra of **7b–7d**, in each case, at the highest field, exhibited a multiplet integrating for two protons in the region at δ 1.84–1.95 ascribable to C_5-methylene protons which was followed by a two-proton multiplet in the region at δ 2.78–2.96 due to C_4-methylene protons. Downward to the resonance in the region at δ 2.78–2.96 was located a multiplet integrating for two protons in the region at δ 3.41–3.49 which accounts for C_6-methylene protons. The N-H proton, however, was appeared as a broad singlet (exchangeable with D_2O) in the region at δ 5.64–6.12. The most characteristic feature of ^{1}H NMR spectra of **7b–7d**, was the resonance of vinylic proton (C_β-H) in the region at δ 7.78–7.90 similar to that observed in lactam (**7a**). The signals due to the remaining aliphatic and aromatic protons were observed in the expected regions (*vide experimental*). In the ^{13}C NMR spectra of **7b–7d**, the signals due to the aliphatic ring carbons, *i.e.* C_5, C_4 and C_6 were observed in the expected regions at δ 22.86–23.70, δ 29.01–29.69 and δ 42.06–42.61, respectively. The signals appeared in the regions at δ 133.68–135.23 and δ 136.23–137.85 were indubitably assigned to C_β and C_3, respectively. The most characteristic feature of ^{13}C NMR spectra of **7b–7d**, was the appearance of a signal, at the lowest field, in the region at δ 162.42–167.04 which was assigned to C_2 (carbon of C=O). The signals due to the remaining aliphatic and aromatic carbons were observed in the expected regions. The fragmentation pattern in the mass spectra of **7b–7d** was analogous to those observed in **7a** and their analytical data were found in good agreement with their molecular formulae (*vide experimental*). All the above assignments are in accord with the earlier observations reported in the literature [50,51,54–58] for structural assignment of these compounds. It is worthy to mention here that Bose *et al* [56] have reported the synthesis of **7a** from the reaction of *N*-acetylpiperidin-2-one with benzaldehyde in presence of NaH/THF. Campi *et al* [50] have synthesized **7a–7c** by the reaction of the 5-arylpent-4-ynylamine (Aryl = C_6H_5, C_6H_4-CH_3(*p*), C_6H_4-OCH_3(*p*)) with H_2/CO in the presence of $[Rh(OAc)_2]_2/PPh_3$ in either benzene or ethyl acetate at 80–90°C for 20h in moderate yields. Hutchinson *et al* [57] have reported the synthesis of **7a** and **7d** by the reaction of 3-diazopiperidin-2-one with corresponding aromatic aldehydes in the presence of triphenylphosphine, methyl trioxorhenium and THF by stirring at room temperature. Liu *et al* [51] reported the synthesis of **7a–7d** by treatment of piperidin-2-one with trifluoroacetic anhydride (TFAA)/toluene followed by reaction wth the corresponding 4-substituted benzaldehydes in presence of potassium *t*-butoxide/THF. Yue *et al* [54] have synthesized **7c** following exactly the same procedure as described by Liu *et al* [51].

In principle, the Beckmann rearrangement of (1*E*,2*E*)-2-arylidenecyclopentanone *O*-tosyl oximes (**6**) are expected to furnish **7** through alkyl migration in which configuration around C=C is (*E*), **8** by alkyl migration in which configuration around C=C is (*Z*), **9** by vinyl migration in which configuration around C=C is (*E*) and **10** by vinyl migration in which configuration around C=C is (*Z*) (Scheme 3).



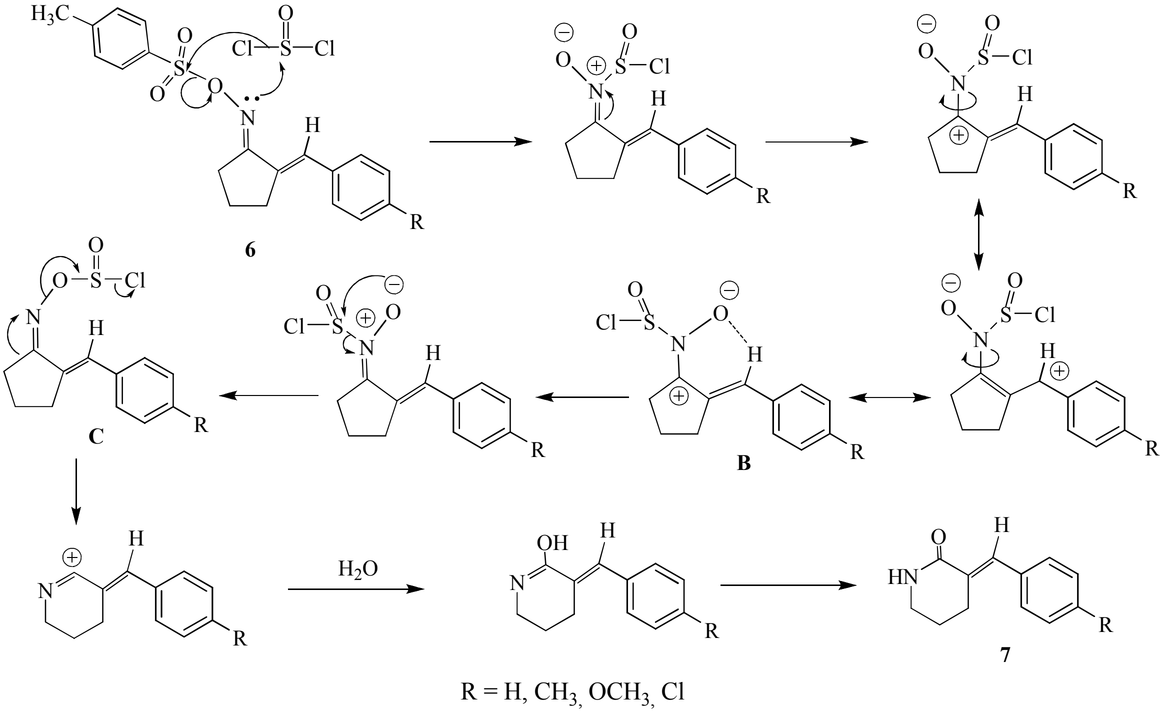
Scheme 3: Expected products of Beckmann rearrangement of (1*E*,2*E*)-2-arylidenecyclopentanone *O*-tosyl oximes (6)

The vinylic proton (C_β-H) in the products formed, *i.e.* **7a–7d** resonates in the lower field in the region at δ 7.78–7.90. If the products would have alternate structures, *i.e.* **8** or **9** or **10**, than C_β-H must have resonated at a comparatively higher field, because it will not lie in the deshielding zone of C=O group in these cases. Therefore, downfield shifting of C_β-H unequivocally proves the formation of **7** and the formation of lactams **8**, **9** and **10** stands rejected.

One more interesting point which deserves attention here is that during the Beckmann rearrangement of *O*-tosyl oximes (**6**), there occurs no movement of *α,β*-unsaturated double bond from exocyclic to endocyclic position to furnish lactam, i.e. 3-benzyl-5,6-dihydropyridin-2(1*H*)-one (**11**). If this migration had happened, it must have exhibited a two-proton signal due to C_3-benzylic CH_2-group and a resonance characteristic of the C_4-vinylic proton but no such type of resonances were observed in ^{1}H NMR spectrum of the product formed.

Hence, all these arguments support the formation of **7** by alkyl migration in which configuration around C=C bond is retained during the Beckmann rearrangement of **6** without shifting of double bond from exocyclic to endocyclic position.

Mechanistically, the conversion of **6** → **7** is envisaged to occur through an initial thionyl chloride catalyzed isomerization around C=N to afford **C** (Scheme 4). Driving force for this isomerization is presumably the stabilization of the intermediate carbocation (**B**) through H-bonding between O^- and H-atom of the C_β-H. The intermediate **C** thus obtained subsequently underwent *anti* migration of alkyl group to afford the lactam **7**.



Scheme 3: Mechanistic pathway for the synthesis of (*E*)-3-arylidenepiperidin-2-ones (7)

CONCLUSION

From the above discussion, it is concluded that the Beckmann rearrangement of (1*E*,2*E*)-2-arylidenecyclopentanone *O*-tosyl oximes (**6a–6d**) catalyzed by thionyl chloride in presence of dry dioxane leads to exclusive formation of the corresponding lactams, *i.e.* (*E*)-3-arylidenepiperidin-2-ones (**7a–7d**) in moderate yields by alkyl migration without shifting of double bond from exocyclic to endocyclic position.

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