Available online at www.derpharmachemica.com

ISSN 0975-413X
CODEN (USA): PCHHAX

Der Pharma Chemica, 2016, 8(17):190-199
(http://derpharmachemica.com/archive.html)

Synthesis of some (*E*)-3-arylidene-3,4-dihydroquinolin-2(1*H*)-ones *via* Schmidt rearrangement

Satbir Mor* and Preeti Pahal

Department of Chemistry, Guru Jambheshwar University of Science & Technology, Hisar-125001, Haryana, India

---

ABSTRACT

*In the present study, synthesis of some (E)-3-arylidene-3,4-dihydroquinolin-2(1H)-ones (**4**) derived from 2,3-dihydro-1H-inden-1-one (**1**) via NaN_3/H_2SO_4 mediated Schmidt rearrangement in moderate yields has been reported. The rearrangement occurred by aryl migration without shifting of double bond from exocyclic to endocyclic position. The structural substantiation of the synthesized compounds was carried out by means of spectral (IR, NMR and mass) as well as elemental analysis results.*

Keywords: Schmidt rearrangement; (*E*)-2-arylidene-2,3-dihydro-1*H*-inden-1-ones; (*E*)-3-arylidene-3,4-dihydroquinolin-2(1*H*)-ones.

INTRODUCTION

Quinolin-2(1*H*)-one and its derivatives are interesting structural motifs which are found in many naturally and non-naturally occurring compounds [1]. Various compounds containing the quinolinone moiety as a key structural feature possess different types of biological properties [2] which have gained the attention of several researchers worldwide. Similarly, 3,4-dihydroquinolin-2(1*H*)-one scaffold is found to be a crucial element in many pharmacologically and biologically active compounds [3]. They have also received considerable attention as precursors of some other biologically active compounds [4]. Quinolinone derivatives exhibit a wide range of applications in medicine [5] and agriculture [6]. They are found as antioxidant and antiulcer agent [7], *β*-adrenergic blocking agent [8], antidepressants [9], effective against various types of cancers and autoimmune disorders such as multiple sclerosis (MS), rheumatoid arthritis, systemic lupus erythematosis, and autoimmune encephalomyelitis [10], bronchial asthma [11], peripheral vascular disease [12], etc. Numerous methods have been developed in the past for the synthesis of quinolinone derivatives [13]. Nevertheless, there always exists a need for developing newer, more efficient and convenient synthetic routes for these types of compounds in view of their wide range of applications. Schmidt rearrangement [14] has since long been recognized as one of the useful methods for the synthesis of *N*-substituted amides and lactams [15]. The various aspects of chemistry of Schmidt rearrangement have been extensively reviewed by different researchers [16]. Moreover, this transformation also finds many applications in the synthesis of a variety of heterocyclic compounds [17], alkaloids [18], and aza steroids [19]. Although literature records spate of publications on Schmidt rearrangement of a variety of saturated cyclic ketones, chemists in the past have exhibited only sporadic attention on the Schmidt rearrangement of *α*,*β*-unsaturated ketones. Considering this and in continuation of our research on nitrogen containing heterocycles [20], in this research paper, we wish to report the synthesis of several (*E*)-3-arylidene-3,4-dihydroquinolin-2(1*H*)-ones (**4**) by Schmidt rearrangement of (*E*)-2-arylidene-2,3-dihydro-1*H*-inden-1-ones (**3**) which, in turn, were derived from 2,3-

dihydro-1*H*-inden-1-one (**1**). Our main aim in the present investigation was to examine whether (i) ketones (**3**) undergo aryl or vinyl migration, and (ii) the rearrangement is accompanied by movement of double bond from exocyclic to endocyclic position or not.

MATERIALS AND METHODS

2.1 General: The chemicals (AR and LR grade) used in the present investigation were procured from Sigma-Aldrich, Qualigens, CDH and Spectrochem. All the solvents were used as such or after necessary purification in accord with the standard literature procedures. The synthesis of different compounds was achieved by stirring on a magnetic stirrer and/or heating on a water bath/ heating mantle. Melting points (mp °C) of the synthesized compounds were determined on an electrothermal apparatus in open head capillaries and are uncorrected. Purity of all the synthesized compounds was checked by thin layer chromatography (TLC) using precoated silica gel (HF_{254}, 200 mesh) plates as stationary phase and different combinations of solvents as mobile phase. The visualization of the spots was carried out by using UV chamber and iodine adsorption. The progress of the reaction, in each case, was also monitored by TLC on aliquots of reaction mixture withdrawn at different intervals of time. The synthesized compounds were characterized by employing different spectral (IR, NMR, Mass) and elemental analytical techniques. IR spectra of the synthesized compounds were scanned on Perkin Elmer Spectrum, BX II FTIR spectrometer using potassium bromide (KBr) pellets and absorption frequencies (ν) are stated in cm^{-1}. The intensities of absorptions are presented as follows: *s*, strong; *m*, medium; *w*, weak. The ^{1}H NMR and ^{13}C NMR spectra of the synthesized compounds were recorded on Bruker Advance 300/400 MHz spectrometer at 300/400 MHz and 75/100 MHz, respectively in $CDCl_3$ The chemical shifts are reported in parts per million (δ ppm) using tetramethylsilane (TMS) as an internal standard. The peak patterns are indicated as follows: s, singlet; br s, broad singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublets. The coupling constant (*J*) values are reported in Hertz (Hz). Mass spectra were recorded on Agilent 6310 LCMS ION TRAP spectrometer. The figure given in the parenthesis represents relative intensity corresponding to the base peak taken as 100. Elemental analyses were performed on Vario Micro Cube Elementar CHNS analyser. Elemental analytical results for C, H and N were found within ±0.4% of the theoretical values.

2.2 General procedure for the synthesis of (*E*)-2-arylidene-2,3-dihydro-1*H*-inden-1-ones (3): To a solution of 2,3-dihydro-1*H*-inden-1-one (**1**, 1.32 g, 0.01 mole) and an appropriate 4-substituted benzaldehyde (**2**, 0.01 mole) in ethanol (150 mL) was added NaOH solution (30 mL, 6.7 M) drop wise while stirring on a magnetic stirrer by keeping the temperature below 5 °C. The crude product precipitated out from the reaction mixture within a few minutes. The stirring was continued for further 30 min. at room temperature. The solid thus obtained was filtered, washed with cold ethanol and then with water until the pH of the wash out was neutral, dried and purified by crystallization from ethanol to furnish the corresponding (*E*)-2-arylidene-2,3-dihydro-1*H*-inden-1-ones (**3**) [21] in high 84% yields. The characterization data of the compounds (**3a–3f**) are given below.

(*E*)-2-(4-bromobenzylidene)-2,3-dihydro-1*H*-inden-1-one (3a)
Yield 84%, mp 180–183 °C (Lit. [22] mp 184.5 °C); IR (KBr, cm^{-1}): 1693 (*s*, C=O, str.), 1606 (*s*, C=C, str.), 1502, 1412, 1366, 1320, 1147, 1052, 856, 741, 623, 547; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.02 (s, 2H, 3-H), 7 .39 (d, 2H, *J* = 8.4 Hz, 3′-H & 5′-H), 7.45–7.76 (m, 6H, 4-H, 5-H, 6-H, 2′-H, 6′-H, H_β), 7.86 (d, 1H, *J* = 7.6 Hz, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 32.36 (C_3), 123.26, 124.05, 126.25, 127.40, 128.51, 130.87, 132.62, 133.74, 133.96, 134.16, 137.85, 149.38 (C_{3a}), 194.10 (C_1).

(*E*)-2-(4-ethylbenzylidene)-2,3-dihydro-1*H*-inden-1-one (3b)
Yield 80.3%, mp 160–162 °C [23]; IR (KBr, cm^{-1}): 1695 (*s*, C=O, str.), 1612 (*s*, C=C, str.), 1606, 1554, 1462, 1319, 1290, 1192, 1097, 954, 837, 736, 677, 555; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.28 (t, 3H, *J* = 7.52 Hz, 4′-$CH_2\underline{CH_3}$), 2.69 (q, 2H, *J* = 7.52 Hz, 4′-$\underline{CH_2}CH_3$), 4.09 (s, 2H, 3-H), 7.29–7.58 (m, 5H, 4-H, 5-H, 6-H, 3′-H, 5′-H), 7.61 (d, 2H, *J* = 7.72 Hz, 2′-H & 6′-H), 7.66 (s, 1H, H_β), 7.89 (d, 1H, *J* = 7.52 Hz, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.31 (4′-$CH_2\underline{C}H_3$), 28.79 (4′-$\underline{C}H_2CH_3$), 32.47 (C_3), 124.27, 126.18, 127.60, 128.51, 130.87, 132.81, 133.80, 133.98, 134.51, 138.08, 146.45, 149.60 (C_{3a}), 194.37 (C_1).

(*E*)-2-(4-methoxybenzylidene)-2,3-dihydro-1*H*-inden-1-one (3c)
Yield 86%, mp 139–141 °C (Lit. [22,24] mp 141 °C); IR (KBr, cm^{-1}): 1694 (*s*, C=O, str.), 1625 (*m*, C=C, str.), 1601, 1515, 1466, 1423, 1257, 1185, 1099, 1024, 957, 822, 734, 673, 525; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.81 (s, 3H, 4′-OCH_3), 4.04 (s, 2H, 3-H), 7.04 (d, 2H, *J* = 8.8 Hz, 3′-H & 5′-H), 7.41–7.76 (m, 6H, 4-H, 5-H, 6-H, 2′-H, 6′-H, H_β),

7.90 (d, 2H, *J* = 7.6 Hz, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 32.35 (C_3), 55.81 (4′-O<u>C</u>H$_3$), 115.02 ($C_{3'}$ & $C_{5'}$), 123.92, 127.07, 128.06, 127.94, 132.99, 133.29, 133.15, 135.06, 137.91, 150.29 (C_{3a}), 161.08 ($C_{4'}$), 193.71 (C_1).

(*E*)-2-(4-nitrobenzylidene)-2,3-dihydro-1*H*-inden-1-one (3d)
Yield 82%, mp 248–250 °C (Lit. [24] mp 251–252 °C); IR (KBr, cm^{-1}): 1695 (*s*, C=O, str.), 1612 (*m*, C=C, str.), 1608, 1564, 1496, 1419, 1292, 1170, 1024, 854, 758, 636, 586; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.09 (s, 2H, 3-H), 7.43–7.89 (m, 4H, 4-H, 5-H, 6-H, H$_\beta$), 7.94 (d, 1H, *J* = 7.6 Hz, 7-H), 8.08 (d, 2H, *J* = 8.80 Hz, 2′-H & 6′-H), 8.31 (d, *J* = 8.8 Hz, 3′-H & 5′-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 32.37 (C_3), 123.55, 124.12, 125.03, 126.30, 128.11, 130.87, 131.00, 135.31, 138.48, 141.67, 147.56 ($C_{4'}$), 149.34 (C_{3a}), 193.60 (C_1).

(*E*)-2-(4-(dimethylamino)benzylidene)-2,3-dihydro-1*H*-inden-1-one (3e)
Yield 80.8%, mp 166–168 °C (Lit. [25,26] mp 167–169 °C); IR (KBr, cm^{-1}): 1680 (*s*, C=O, str.), 1611 (*m*, C=C, str.), 1598, 1502, 1498, 1332, 1150, 1035, 1011, 925, 845, 741, 633, 512; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.11 (s, 6H, 4′-N(CH$_3$)$_2$), 3.98 (s, 2H, 3-H), 6.78 (d, 2H, *J* = 8.4 Hz, 3′-H & 5′-H), 7.38–7.73 (m, 6H, 4-H, 5-H, 6-H, 2′-H, 6′-H, H$_\beta$), 7.86 (d, 1H, *J* = 8.0 Hz, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 32.28 (C_3), 40.25 (4′-N(<u>C</u>H$_3$)$_2$), 112.25 ($C_{3'}$ & $C_{5'}$), 123.92, 124.10, 127.94, 128.06, 129.32, 133.15, 133.29, 134.75, 137.86, 149.62 (C_{3a}), 150.92 ($C_{4'}$), 194.11 (C_1).

(*E*)-2-(3-hydroxy-4-methoxybenzylidene)-2,3-dihydro-1*H*-inden-1-one (3f)
Yield 85.4%, mp 175–178 °C [27]; IR (KBr, cm^{-1}): 3410 (*m*, O–H, str.), 1685 (*s*, C=O, str.), 1610 (*m*, C=C, str.), 1517, 1382, 1193, 1076, 968, 858, 742, 621; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.95 (s, 3H, 4′-OCH$_3$), 4.02 (s, 2H, 3-H), 5.81 (br s, 1H, 3′-OH, exchangeable with D_2O), 6.92 (d, 1H, $J_{5'6'}$ = 8.48 Hz, 5′-H), 7.19 (dd, 1H, $J_{6'5'}$ = 8.48 Hz, $J_{6'2'}$ = 1.88 Hz, 6′-H), 7.32 (d, $J_{2'6'}$ = 1.88 Hz, 2′-H), 7.40–7.62 (m, 4H, 4-H, 5-H, 6-H, H$_\beta$), 7.90 (d, 1H, *J* = 7.6 Hz, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 32.46 (C_3), 56.03 (4′-O<u>C</u>H$_3$), 110.74 ($C_{5'}$), 115.67 ($C_{2'}$), 124.33, 124.95, 126.15, 127.59, 129.04, 132.94, 133.98, 134.41, 138.20 (C_2, C_4, C_5, C_6, C_7, C_{7a}, C_β, $C_{1'}$, $C_{6'}$), 145.80 ($C_{3'}$), 148.05 ($C_{4'}$), 149.60 (C_{3a}), 194.44 (C_1).

2.3 General procedure for the synthesis of (*E*)-3-arylidene-3,4-dihydroquinolin-2(1*H*)-ones (4): To a cooled suspension of (*E*)-2-arylidene-2,3-dihydro-1*H*-inden-1-one (**3**, 0.0093 mole) and sodium azide (1.30 g, 0.02 mole) in chloroform (50 mL), was added conc. H_2SO_4 (5 mL) dropwise with continuous stirring on a magnetic stirrer while maintaining the temperature below 40 °C. After the addition was over, the reaction mixture was further stirred at room temperature. The progress of the reaction was monitored through TLC on aliquots withdrawn from the reaction mixture (after neutralization and extraction) at regular intervals of time. After completion of the reaction, contents were cooled and poured into crushed ice. The chloroform layer was separated and aqueous layer was extracted with chloroform (3×50 mL). All the extracts were combined with chloroform layer and dried over anhydrous Na_2SO_4 which upon concentration under reduced pressure furnished a residue that was chromatographed over a column of silica-gel. Elution of the column with hexane:ethyl acetate (95:5, v/v) afforded a solid which upon crystallization from a suitable solvent furnished the corresponding (*E*)-3-arylidene-3,4-dihydroquinolin-2(1*H*)-ones (**4**) in good yields. The characterization data of the compounds (**4a–4f**) are given below.

(*E*)-3-(4-bromobenzylidene)-3,4-dihydroquinolin-2(1*H*)-one (4a)
Time required for completion of reaction 9h; white crystals (ethanol), yield 71%; mp 274–276 °C; IR (KBr, cm^{-1}): 3307 (*m*, N–H, str.), 1664 (*s*, C=O, str.), 1598 (*s*, C=C, str.), 1510, 1477, 1408, 1283, 1171, 1087, 950, 825, 740, 678, 503; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.99 (s, 2H, 4-H), 6.85 (d, 1H, *J* = 8.4 Hz, 8-H), 6.99 (d, 1H, *J* = 8.4 Hz, 6-H), 7.13–7.26 (m, 2H, 5-H, 7-H), 7.41 (d, 2H, *J* = 8.4 Hz, 3′-H & 5′-H), 7.58 (d, 2H, *J* = 8.4 Hz, 2′-H & 6′-H), 7.91 (s, 1H, H$_\beta$), 9.57 (br s, 1H, NH, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$): δ 29.70 (C_4), 115.71, 123.41, 124.49, 126.55, 127.80, 130.72, 131.55, 131.98, 134.28, 135.07, 136.33, 137.86, 169.33 (C_2); ESI-MS m/z: 313 ($M^{+\cdot}$, 100)/315 ($M^{+\cdot}$+2, 95), 312 (62.5)/314 (61.3), 296 (25)/298 (24.7), 285 (15.2)/287 (15.4), 233 (12), 170 (6.3)/172 (6), 89 (14); *Anal.* Calcd. for $C_{16}H_{12}BrNO$ (313.01): C, 61.17; H, 3.85; N 4.46. Found: C, 60.92; H, 4.09; N, 4.75.

(*E*)-3-(4-ethylbenzylidene)-3,4-dihydroquinolin-2(1*H*)-one (4b)
Time required for completion of reaction 11h; yellow crystals (benzene), yield 62.2%; mp 192–193 °C; IR (KBr, cm^{-1}): 3269 (*m*, N–H, str.), 1670 (*s*, C=O, str.), 1602 (*s*, C=C, str.), 1512, 1425, 1369, 1220, 1178, 1052, 1002, 908, 840, 745, 698; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.27 (t, 3H, *J* = 7.5 Hz, 4′-CH$_2$<u>CH$_3$</u>), 2.69 (q, 3H, *J* = 7.5 Hz, 4′-<u>CH$_2$</u>CH$_3$), 4.03 (s, 2H, 4-H), 6.83 (d, 1H, *J* = 7.5 Hz, 8-H), 6.96 (d, 1H, *J* = 7.5 Hz, 6-H), 7.06–7.25 (m, 2H, 5-H, 7-

H), 7.29 (d, 2H, *J* = 8.1 Hz, 3′-H & 5′-H), 7.59 (d, 2H, *J* = 8.1 Hz, 2′-H & 6′-H), 7.92 (*s*, 1H, H_{β}), 9.23 (br s, 1H, NH, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.23 (4′-$CH_2\underline{C}H_3$), 27.53 (4′-$\underline{C}H_2CH_3$), 30.71 (C_4), 115.93, 121.64, 123.18, 126.33, 127.52, 130.22, 131.45, 133.52, 134.95, 136.64, 138.23, 146.03, 167.03 (C_2); ESI-MS m/z: 263 ($M^{+\cdot}$, 100), 262 (64.6), 246 (27.1), 235 (16.4), 234 (8.2), 91 (9.6), 89 (13.4), 77 (6.2); *Anal*. Calcd. for $C_{18}H_{17}NO$ (263.13): C, 82.10; H, 6.51; N 5.32. Found: C, 82.41; H, 6.36; N, 5.57.

(*E*)-3-(4-methoxybenzylidene)-3,4-dihydroquinolin-2(1*H*)-one (4c)

Time required for completion of reaction 8h; white crystals (methanol), yield 64.7%; mp 184–187 °C, IR (KBr, cm^{-1}): 3245 (*m*, N–H, str.), 1670 (*s*, C=O, str.), 1606 (*s*, C=C, str.), 1478, 1310, 1214, 1056, 915, 860, 720, 644, 523; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.84 (s, 3H, 4′-OCH_3), 4.06 (s, 2H, 4-H), 6.78 (d, 2H, *J* = 8.1 Hz, 3′-H & 5′-H), 6.89 (d, 1H, *J* = 8.4 Hz, 8-H), 7.18–7.31 (m, 3H, 5-H, 6-H, 7-H), 7.36 (d, 2H, *J* = 8.1 Hz, 2′-H & 6′-H), 7.79 (s, 1H, H_{β}), 8.57 (br s, 1H, NH, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$): δ 30.63 (C_4), 56.03 (4′-$O\underline{C}H_3$), 113.62, 114.98, 121.63, 123.82, 128.33, 130.70, 131.55, 134.28, 135.07, 136.33, 139.41, 156.23 ($C_{4'}$), 165.32 (C_2); ESI-MS m/z: 265 ($M^{+\cdot}$, 100), 264 (65.3), 250 (8.3), 248 (32.7), 237 (12), 222 (27), 121 (7), 91 (5.3), 89 (20.4); *Anal.* Calcd. for $C_{17}H_{15}NO_2$ (265.11): C, 76.96; H, 5.70; N 5.28. Found: C, 77.09; H, 5.41; N, 5.54.

(*E*)-3-(4-nitrobenzylidene)-3,4-dihydroquinolin-2(1*H*)-one (4d)

Time required for completion of reaction12h; yellow crystals (methanol), yield 59%; mp 250–254 °C; IR (KBr, cm^{-1}): 3325 (*m*, N–H, str.), 1662 (*s*, C=O, str.), 1596 (*s*, C=C, str.), 1478, 1326, 1288, 1172, 1146, 1025, 996, 745, 612, 502; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.99 (s, 2H, 4-H), 6.84 (d, 1H, *J* = 8.1 Hz, 8-H), 6.94–7.27 (m, 3H, 5-H, 6-H, 7-H), 7.84 (s, 1H, H_{β}), 8.07 (d, 2H, *J* = 8.4 Hz, 2′-H & 6′-H), 8.32 (d, *J* = 8.8 Hz, 3′-H & 5′-H), 9.85 (br s, 1H, NH, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$): δ 30.53 (C_4), 114.86, 122.56, 124.38, 126.37, 127.46, 130.56, 131.60, 136.12, 138.13, 139.65, 142.35, 147.23 ($C_{4'}$), 167.26 (C_2); ESI-MS m/z: 280 ($M^{+\cdot}$, 100), 279 (70), 263 (35.6), 252 (15.2), 250 (11), 222 (25), 123 (14.2), 89 (22.4). *Anal.* Calcd. for $C_{16}H_{12}N_2O_3$ (280.08): C, 68.56; H, 4.32; N 9.99. Found: C, 68.27; H, 4.62; N, 9.71.

(*E*)-3-(4-(dimethylamino)benzylidene)-3,4-dihydroquinolin-2(1*H*)-one (4e)

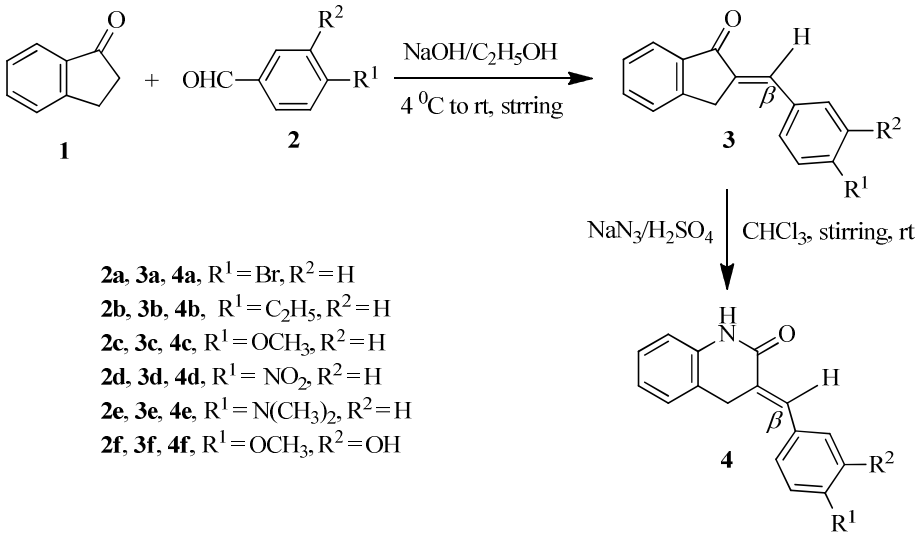
Time required for completion of reaction 12h; yellow crystals (benzene), yield 70%; mp 290–292 °C; IR (KBr, cm^{-1}): 3295 (*m*, N–H, str.), 1660 (*s*, C=O, str.), 1603 (*s*, C=C, str.), 1523, 1440, 1363, 1224, 1192, 1107, 958, 817, 731, 528; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.07 (s, 6H, 4′-$N(CH_3)_2$), 4.09 (s, 2H, 4-H), 6.75 (d, 2H, *J* = 8.7 Hz, 3′-H & 5′-H), 6.87–7.01 (m, 2H, 6-H, 8-H), 7.11–7.30 (m, 2H, 5-H, 7-H), 7.64 (d, 2H, *J* = 8.7 Hz, 2′-H & 6′-H), 7.85 (s, 1H, H_{β}), 10.11 (br s, 1H, NH, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$): δ 32.28 (C_4), 40.25 (4′-$N(\underline{C}H_3)_2$), 111.92, 115.40, 121.86, 122.93, 124.11, 127.91, 130.78, 131.56, 135.52, 137.58, 140.23, 149.23 ($C_{4'}$), 166.45 (C_2); ESI-MS m/z: 278 ($M^{+\cdot}$, 100), 277 (64.5), 261 (36), 250 (14.5), 89 (23.4); *Anal*. Calcd. for $C_{18}H_{18}N_2O$ (278.14): C, 77.67; H, 6.52; N 10.06. Found: C, 77.38; H, 6.75; N, 9.84.

(*E*)-3-(3-hydroxy-4-methoxybenzylidene)-3,4-dihydroquinolin-2(1*H*)-one (4f)

Time required for completion of reaction 11h; white crystals (ethanol), yield 68.6%; mp 214–216 °C; IR (KBr, cm^{-1}): 3361 (*m*, O–H, str.), 3219 (*m*, N–H, str.), 1668 (*s*, C=O, str.), 1595 (*s*, C=C, str.), 1450, 1354, 1143, 995, 877, 619; ^{1}H NMR (300MHz, $CDCl_3$): δ 3.78 (s, 3H, 4′-OCH_3), 4.06 (s, 2H, 4-H), 5.82 (br s, 1H, 3′-OH, exchangeable with D_2O), 6.86 (d, 1H, $J_{5'6'}$ = 8.7 Hz, 5′-H), 6.92–7.29 (m, 4H, 5-H, 6-H, 7-H, 8-H), 7.26 (dd, 1H, $J_{6'5'}$ = 8.7 Hz, $J_{6'2'}$ = 2.4 Hz, 6′-H), 7.36 (d, 1H, $J_{2'6'}$ = 1.88 Hz, 2′-H), 7.76 (s, 1H, H_{β}), 10.03 (br s, 1H, NH, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$): δ 29.83 (C_4), 56.12 (4′-$O\underline{C}H_3$), 112.98 ($C_{5'}$), 114.67 ($C_{2'}$), 115.46, 120.56, 122.65, 124.03, 127.52, 128.45, 134.87, 137.12, 139.08, 140.12, 145.23 ($C_{3'}$), 156.23 ($C_{4'}$), 166.35 (C_2); ESI-MS m/z: 281 ($M^{+\cdot}$, 100), 280 (60.2), 264 (35.4), 253 (13.4), 89 (22.6); *Anal*. Calcd. for $C_{17}H_{15}NO_3$ (281.11): C, 72.58; H, 5.37; N, 4.98. Found: C, 72.80; H, 5.56; N, 5.21.

RESULTS AND DISCUSSION

The strategy towards the synthesis of quinolinones (**4**) involves an initial condensation of 2,3-dihydro-1*H*-inden-1-one (**1**) with appropriate benzaldehydes (**2**) in base-catalyzed conditions to give (*E*)-2-arylidene-2,3-dihydro-1*H*-inden-1-ones (**3a**–**3f**), which upon subsequent Schmidt rearrangement with NaN_3/H_2SO_4 furnished the corresponding (*E*)-3-arylidene-3,4-dihydroquinolin-2(1*H*)-ones (**4a**–**4f**) in good yields (59–71%) (Scheme 1).



Scheme 1

The 2,3-dihydro-1*H*-inden-1-one (**1**) is commercially available and was procured from Sigma-Aldrich. The (*E*)-2-arylidene-2,3-dihydro-1*H*-inden-1-ones (**3a**–**3f**) were prepared by the condensation of 2,3-dihydro-1*H*-inden-1-one (**1**) with appropriate 4-substituted benzaldehydes (**2a**–**2f**) in the presence of $NaOH/C_2H_5OH$ by stirring in high yields (80.3–86%) following the procedure as described in literature [21]. IR spectra of the entire synthesized (*E*)-2-arylidene-2,3-dihydro-1*H*-inden-1-ones (**3a**–**3f**) exhibited characteristic absorptions due to C=C and C=O stretchings in the regions at 1606–1625 cm^{-1} and 1680–1695 cm^{-1}, respectively [23]. The ^1H NMR spectra of arylidenes (**3a**–**3f**), in each case, showed a characteristic one-proton doublet (J = 7.52–7.80) in the region at δ 7.86–7.94 due to C_7-H besides other aromatic and non-aromatic proton resonances. The most distinguishing feature of ^{13}C NMR spectra of **3a**–**3f** is the presence of a signal in the region at δ 193.15–194.73 ascribable to C_1 [28]. Another noteworthy feature is the appearance of a signal in the region at δ 149.34–154.97 which was assigned to C_{3a}. The signals due to the remaining carbons were appeared in the expected regions (*vide* experimental).

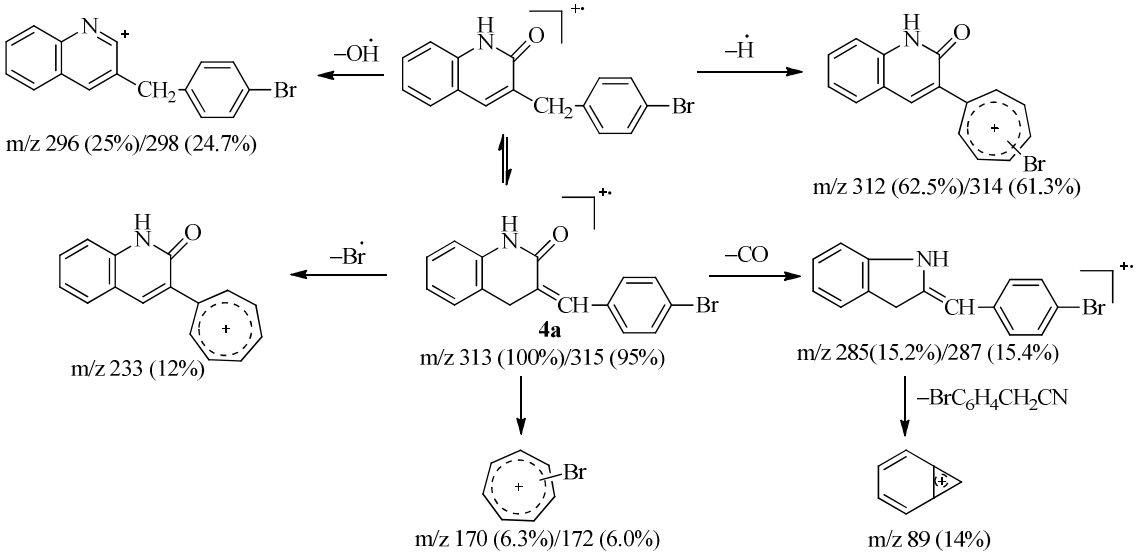
All the (*E*)-2-arylidene-2,3-dihydro-1*H*-inden-1-ones (**3**) were next converted into their corresponding (*E*)-3-arylidene-3,4-dihydroquinolin-2(1*H*)-ones (**4**) by Schmidt rearrangement. Initially, to a cooled suspension of (*E*)-2-(4-bromobenzylidene)-2,3-dihydro-1*H*-inden-1-one (**3a,** 2.771 g, 0.0093 mole) and sodium azide (1.30 g, 0.02 mole) in chloroform (50 mL), was carefully added conc. H_2SO_4 (5 mL) dropwise with continuous stirring while maintaining the temperature below 40 °C. After the addition was over, the reaction mixture was further stirred at room temperature for 9h by which time TLC analysis of the reaction mixture revealed complete disappearance of the starting material. The usual work up of the resulting reaction mixture afforded a residue which was chromatographed over a column of silica-gel. Elution of the column with hexane-ethyl acetate (95:5, v/v) gave a solid which was crystallized from ethanol to afford (*E*)-3-(4-bromobenzylidene)-3,4-dihydroquinolin-2(1*H*)-one (**4a**) as white crystals in 71% yield, mp 274–276 °C.

The structure of **4a** was established on the basis of its spectral (IR, ^1H NMR, ^{13}C NMR and mass) as well as elemental analysis results. IR spectrum of **4a**, displayed an absorption band of medium intensity at 3307 cm^{-1} due to N–H stretching of secondary amide. Another noteworthy feature was the presence of two strong bands at 1664 cm^{-1} and 1598 cm^{-1} due respectively to C=O and C=C stretchings of *α*,*β*-unsaturated amide group as found in analogous 3,4-dihydroquinolinones [29]. The ^1H NMR (300 MHz, $CDCl_3$) spectrum of **4a**, in the aliphatic region displayed a two-proton singlet at δ 3.99 ascribable to the protons located at C_4. Next towards the lower field, was observed a one-proton doublet (J = 8.40 Hz) at δ 6.85 due to C_8-H. It was followed by another doublet (J = 8.40 Hz) integrating for one proton due to C_6-H which appeared at δ 6.99. The signal due to C_5-H and C_7-H was observed as a two-proton multiplet in the region at δ 7.13–7.26. All these assignments find support from the results reported in literature for ^1H NMR spectra of analogous compounds [29–31]. Next, towards the lower field, in the aromatic region of spectrum, was observed a two-proton doublet (J = 8.40 Hz) at δ 7.41 ascribable to $C_{3'}$-H and $C_{5'}$-H followed by another doublet (J = 8.40 Hz) integrating for two protons located at δ 7.58 easily assigned to $C_{2'}$-H and $C_{6'}$-H. At the lowest field of the spectrum, was located a one-proton singlet at δ 7.91 attributable to vinylic proton,

i.e. C_{β}-H in accord with the results reported in literature for similar protons in analogous compounds [29]. The N-H proton, however, was observed as a broad singlet (exchangeable with D_2O) at δ 9.57.

The structure of **4a** was further supported by its ^{13}C NMR spectrum, which showed signals due to fourteen magnetically non-equivalent carbons. In the highest field of the spectrum, was observed a signal at δ 29.70 which was undoubtedly assigned to C_4. However, the signal displayed at the lowest field of the spectrum at δ 169.33 was easily assigned to carbonyl carbon, *i.e.* C_2. These assignments rest upon the results reported in literature for ^{13}C NMR spectra of analogous quinolinone derivatives [29]. The remaining carbons of quinolinone part and 4-bromobenzylidene group, *i.e.* C_3, C_{4a}, C_5, C_6, C_7, C_8, C_{8a}, C_{β}, $C_{1'}$, $C_{2',6'}$, $C_{3',5'}$, and $C_{4'}$ displayed signals at δ 115.71, δ 123.41, δ 124.49, δ 126.55, δ 127.80, δ 130.72, δ 131.55, δ 131.98, δ 134.28, δ 135.07, δ 136.33 and δ 137.86.

Furthermore, the structure of **4a** was confirmed by its mass spectrum which showed the expected isotopic peaks in the ratio 1:1 due to the presence of one bromine atom in the molecule. The molecular ion ($M^{+\cdot}$) peak was observed as base peak at m/z 313 (100%)/315 (95%). The next abundant peak ($M^{+\cdot}$-1) was located at m/z 312 (62.5%)/314 (61.3%) which corresponds to the loss of a hydrogen atom molecular ion probably from the benzylic methylene group. A noteworthy feature of the mass spectrum of **4a** was the elision of $OH^{\cdot}$ (17 mass units) from the molecular ion to give ion peak at m/z 296 (25%)/298 (24.7%). The most plausible contender for this ion peak is 3-(4-bromobenzyl)quinolinium cation. Further, the sequential loss of CO (28 mass units) and 4-$BrC_6H_4CH_2C{\equiv}N$ (196 mass units) from the molecular ion furnished ion peaks at m/z 285 (15.2%)/287 (15.4%) and m/z 89 (14%), respectively. Direct loss of bromine atom from the molecular ion furnished an ion peak at 233 (12%). An ion peak of relatively low abundance was also obtained due to bromotropylium cation at m/z 170 (6.3%)/172 (6.0%). The genesis of all these peaks is sketched in Scheme 2.



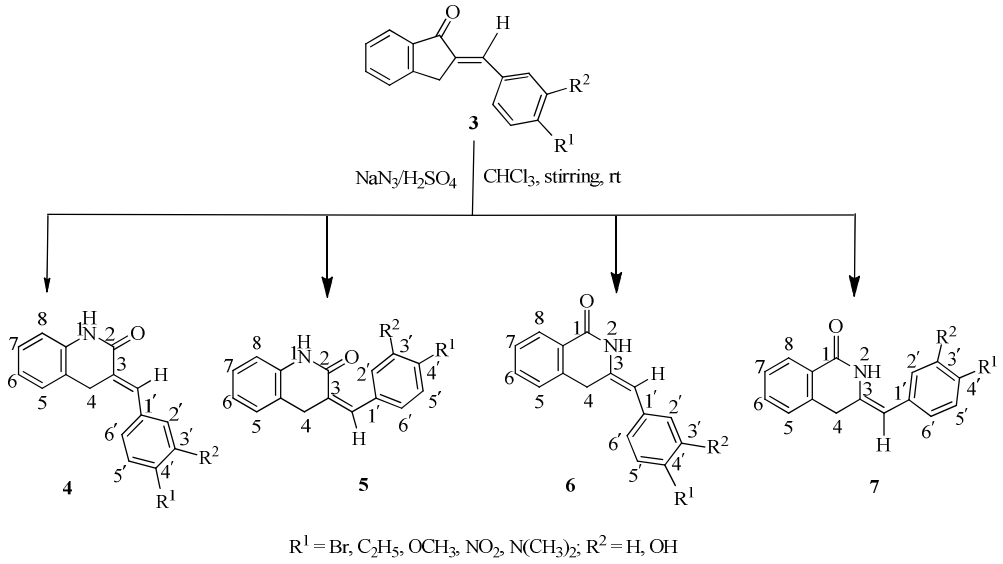
Scheme 2

Additionally, the elemental analysis result of **4a** was found in consistent with its molecular formula. *Anal.* Calcd. for $C_{16}H_{12}BrNO$ (313.01): C, 61.17; H, 3.85; N 4.46. Found: C, 60.92; H, 4.09; N, 4.75.

To explore the generality of the reaction, the Schmidt rearrangement of the remaining arylidenes (**3b**–**3f**) was carried out under similar reaction conditions as employed for **3a.** Here again, the usual work up of the reaction mixture yielded the corresponding (*E*)-3-arylidene-3,4-dihydroquinolin-2(1*H*)-ones (**4b**–**4f**) in good yields (59–70%). The structures of all the products thus obtained were corroborated on the basis of their spectral (IR, ^1H NMR, ^{13}C NMR and mass) and elemental analysis data. IR spectra of **4b**–**4f**, in each case, exhibited the characteristic medium intensity absorption band in the region at 3219–3325 cm^{-1} due to N–H stretching of secondary amide. The two strong absorption bands observed in the regions at 1660–1670 cm^{-1} and 1595–1606 cm^{-1} were assigned to C=O stretching and C=C stretching, respectively. The ^1H NMR spectra of **4b**–**4f**, in each case, displayed a two-proton singlet in the region at δ 4.03–4.21 which could safely be assigned to the protons located at C_4. In **4b**–**4d**, the one-

proton doublet (J = 7.50–8.40 Hz) due to C_8-H was observed in the region at δ 6.83–6.89 while in **4e**, the resonance due to C_8-H got merged with C_6-H which were appeared as a two-proton multiplet in the region at δ 6.87–7.01. In **4b**, C_6-H was observed as a one- proton doublet (J = 7.50 Hz) at δ 6.96 while the signal due to C_5-H and C_7-H was observed as a multiplet integrating for two protons in the region at δ 7.06–7.25. In **4c** and **4d**, the signal due to C_5-H, C_6-H and C_7-H was observed as a three-proton multiplet in the region at δ 6.94–7.31whereas in **4e**, a two-proton multiplet observed in the region at δ 7.11–7.30 was assigned to C_5-H and C_7-H. However, in **4f**, the resonances due to C_5-H, C_6-H, C_7-H and C_8-H were appeared as a four-proton complex multiplet in the region at δ 6.92–7.29. At the lowest field, in ^{1}H NMR spectra of **4b**–**4f**, in each case, was located a one-proton singlet in the region at δ 7.76–7.92 attributable to vinylic proton (C_β-H). Further, the N-H proton was observed as a broad singlet (exchangeable with D_2O) in the region at δ 8.57–10.11. The signals due to the remaining aromatic and aliphatic protons were observed in the expected regions. The ^{13}C NMR spectra of **4b**–**4f**, in each case, in the aliphatic region, exhibited a signal in the region at δ 29.83–32.28 attributable to C_4. Another characteristic feature was the presence of a signal in the most downfield region at δ 165.32–167.26 which was indubitably assigned to C_2. The signals due to the remaining aromatic and aliphatic carbons were observed in the expected regions. Further, the mass spectra of **4b**–**4f** showed the expected fragmentation pattern and their elemental analysis data were also found in good agreement with their molecular formulae (*vide* experimental).

In principle, Schmidt rearrangement of (*E*)-2-arylidene-2,3-dihydro-1*H*-inden-1-ones (**3a**–**3f**) is expected to furnish **4a**–**4f** (by aryl migration in which configuration around C=C is (*E*)), **5** (by aryl migration in which configuration around C=C is (*Z*)), **6** (by vinyl migration in which configuration around C=C is (*E*)) and **7** (by vinyl migration in which configuration around C=C is (*Z*)) (Scheme 3). A distinction between these structures has been made on the basis of ^{1}H NMR spectral studies.

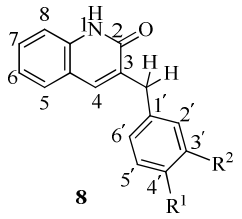


Scheme 3

If the isoquinolinones, **6** and **7** had been obtained by Schmidt rearrangement of (*E*)-2-arylidene-2,3-dihydro-1*H*-inden-1-ones (**3a**–**3f**) through vinyl migration, then C_8-H must have resonated in the downfield region in their ^{1}H NMR spectra as evidenced earlier by Blanco *et al.* [32] in analogous isoquinolinones in which similar proton appears at δ 8.15. However, no such signal in the downfield region was observed in the isolated products **4a**–**4f**, and C_8-H appeared in the region at 6.85–7.29, therefore, formation of **6** and **7** stands rejected. On the other hand, if the quinolinones (**4**) have an alternate structure, *i.e.* **5**, in which configuration around C=C is (*Z*), then the signal due C_β-H might have appeared in somewhat an upfield region in its ^{1}H NMR spectrum [33]. Therefore, the appearance of C_β-H relatively in a downfield region supports the structure **4** for the product of Schmidt rearrangement of **3** and formation of **5** also stands rejected.

One more interesting point which deserves attention here is that during the Schmidt rearrangement of **3**, the possibility of movement of *α,β*-unsaturated double bond from exocyclic to endocyclic position to furnish

quinolinone (**8**) can not be avoided. 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 in the ^{1}H NMR spectrum of the product formed but no such type of resonances were observed in the present investigation. Thus, it can be stated without any reservation that there occurs no movement of *α,β*-unsaturated double bond from exocyclic to endocyclic position during the Schmidt rearrangement of (*E*)-2-arylidene-2,3-dihydro-1*H*-inden-1-ones (**3**).

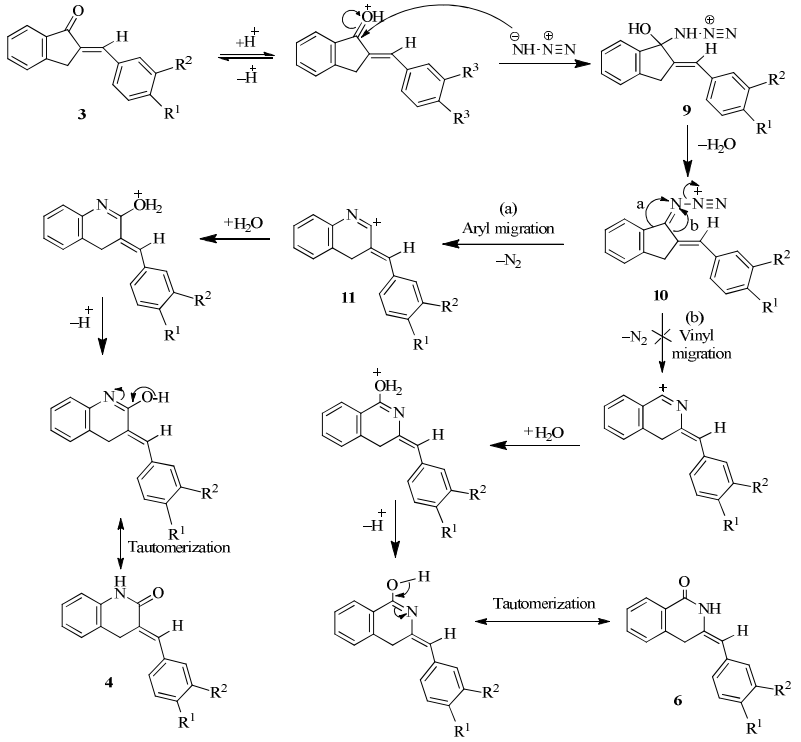


8

R^1 = Br, C_2H_5, OCH_3, NO_2, $N(CH_3)_2$
R^2 = H, OH

All these arguments support the formation of (*E*)-3-arylidene-3,4-dihydroquinolin-2(1*H*)-ones (**4**) by Schmidt rearrangement of (*E*)-2-arylidene-2,3-dihydro-1*H*-inden-1-ones (**3**) through aryl migration in which configuration around C=C bond is retained.

Mechanistically, the transformation of **3** → **4** is envisaged to occur through an initial protonation of carbonyl group followed by nucleophillic attack by the nitrogen of hydrazoic acid to afford the intermediate (**9**) which subsequently loses a molecule of water to furnish **10** that subsequently undergoes aryl migration to furnish carbocation (**11**). The carbocation (**11**) upon nucleophillic attack by H_2O followed by loss of a proton and subsequent tautomerization affords the quinolinone (**4**) (Scheme 4).



R^1 = Br, C_2H_5, OCH_3, NO_2, $N(CH_3)_2$; R^2 = H, OH

Scheme 4

CONCLUSION

From the above discussion, it is evident that during the NaN_3/H_2SO_4 mediated Schmidt rearrangement of (*E*)-2-arylidene-2,3-dihydro-1*H*-inden-1-ones (**3**) at normal temperature under stirring, exclusively aryl migration has

occurred without shifting of the exocyclic double bond to endocyclic position thereby affording (*E*)-3-arylidene-3,4-dihydroquinolin-2(1*H*)-ones (**4**) in moderate yields.

Acknowledgments
The authors gratefully acknowledge Council of Scientific and Industrial Research (CSIR), New Delhi for generous financial grants [No. 09/752(0012)/2007-EMR-1].

REFERENCES

[1] K. Undheim, T. Benneche, 'In Comprehensive Heterocyclic Chemistry II' (A.R. Katritzky, C.W. Rees, E.F.V. Scriven, A. McKillop, Eds.); Pergamon: Oxford, **1996**, 6, 93–231.
[2] (a) K. Faber, T. Kappe, *J. Heterocycl. Chem.*, **1984**, 21, 881–1883; (b) I.V. Ukrainets, S.G. Taran, O.A. Evtifeeva, A.V. Turov, *Khim. Geterotsikl. Soedin.*, **1993**, 8, 1101–1104; (c) R. Uchida, R. Imasato, Y. Yamaguchi, R. Masuma, K. Shiomi, H. Tomoda, S. Omura, *J. Antibiot. (Tokyo)*, **2005**, 58, 804–809; (d) R.V. Kumar, K.R. Gopal, K.V.S.R.S. Kumar, *J. Heterocycl. Chem.*, **2005**, 42, 1402–1408; (e) Z. Xiao, N.C. Waters, C.L. Woodard, P.K. Li, *Bioorg. Med. Chem. Lett.*, **2001**, 11, 2875–2878; (f) B. Joseph, F. Darro, A. Behard, B. Lesur, F. Collignon, C. Decaestecker, A. Frydman, G. Guillaumet, R. Kiss, *J. Med. Chem.*, **2002**, 45, 2534–2555; (g) T. Nishi, Y. Kimura, K. Nakagawa, *Yakugaku Zasshi*, **2000**, 120, 1247–1260; (h) K. Banno, T. Fujioka, T. Kikuchi, Y. Oshiro, T. Hiyama, K. Nakagawa, *Chem. Pharm. Bull.*, **1988**, 36, 4377–4388.
[3] (a) C.H. Liao, C.C. Tzeng, C.M. Teng, *Eur. J. Pharmacol.*, **1998**, 349, 107–114; (b) Y.C. Huang, J.H. Guh, Z.J. Cheng, Y.L. Chang, T.L. Hwang, C.H. Liao, C.C. Tzeng, C.M. Teng, *Eur. J. Pharmacol.*, **2001**, 418, 133–139; (c) Y. Oshiro, Y. Sakurai, S. Sato, N. Kurahashi, T. Tanaka, T. Kikuchi, K. Tottori, Y. Uwahodo, T. Miwa, T. Nishi, *J. Med. Chem.*, **2000**, 43, 177–189; (d) M. Maeda, *Adv. Drug Deliv. Rev.*, **1991**, 6, 181–202; (e) T.A. Engler, K.O. Lynch, W. Chai, S.T. Meduna, *Tetrahedron Lett.*, **1995**, 36, 2713–2716; (f) T. Fujioka, S. Teramoto, T. Mori, T. Hosokawa, T. Sumida, M. Tominaga, Y. Yabuuchi, *J. Med. Chem.*, **1992**, 35, 3607–3612; (g) T. Uno, Y. Ozeki, Y. Koga, G.N. Chu, M. Okada, K. Tamura, T. Igawa, F. Unemi, M. Kido, T. Nishi, *Chem. Pharm. Bull.*, **1995**, 43, 1724–1733.
[4] (a) T.A. Engler, K.O. LaTessa, R. Iyengar, W.Y. Chai, K. Agrios, *Bioorg. Med. Chem.*, **1996**, 4, 1755–1769; (b) J. Marmur, *J. Mol. Biol.*, **1961**, 3, 208–218.
[5] M. Abass, B.B. Mostafa, *Bioorg. Med. Chem.*, **2005**, 13, 6133–6144.
[6] I.A. Khan, G. Hassan, Ihsanullah, M. A. Khan, Asian J. Plant Sci., **2003**, 2, 294–296.
[7] M. Uchida, F. Tabusa, M. Komatsu, S. Morita, T. Kanbe, K. Nakagawa, *Chem. Pharm. Bull.*, **1985**, 33, 3775–3786.
[8] S. Morita, Y. Irie, Y. Saitoh, H. Kohri, *Biochem. Pharmacol.*, **1976**, 25, 1837–1842.
[9] N.R. Pai, D.S. Dubhashi, D. Pusalkar, *Int. J. Pharm. Sci. Rev. Res.*, **2010**, 5, 124–131.
[10] E. Eriksoo, E.B.M. Sandberg, L.J.T. Stahhandske, EP 82-850032 19820222; *Chem. Abstr.* **1982**, 98, 34513.
[11] Y. Aoki, M. Ishiwara, A. Koda, H. Takagaki, *Eur. J. Pharmacol.*, **2000**, 409, 325–330.
[12] T. Nishi, F. Tabusa, T. Tanaka, T. Shimizu, T. Kanbe, Y. Kimura, K. Nakagawa, *Chem. Pharm. Bull.*, **1983**, 31, 1151–1157.
[13] (a) K.Y. Lee, J.N. Kim, *Bull. Korean Chem. Soc.*, **2002**, 23, 939–940; (b) A. Reissert, *Berichte der deutscen Chemischen Gesellschaff*, **1905**, 38, 3415–3435; (c) J. Oble, L. El Kaïm, M. Gizzi, L. Grimaud, *Heterocycles*, **2007**, 73, 503–517.
[14] (a) K.F. Schmidt, *Angew. Chem.*, **1923**, 36, 511–524; (b) K.F. Schmidt, *Ber.*, **1924**, 57, 704–706; (c) J.R. Dice, P.A.S. Smith, *J. Org. Chem.*, **1949**, 14, 179–183; (d) P.A.S. Smith, B. Ashby, *J. Am. Chem. Soc.*, **1950**, 72, 2503–2505; (e) P.A.S. Smith, *J. Am. Chem. Soc.*, **1948**, 70, 320–323; (f) P.A.S. Smith, *J. Am. Chem. Soc.*, **1954**, 76, 431–436; (g) L.H. Briggs, G.C. De Ath, S.R. Ellis, *J. Chem. Soc.*, **1942**, 61–63; (h) L.H. Briggs, J.W. Lyttleton, *J. Chem. Soc.*, **1943**, 421–425.
[15] (a) W.E. McEwen, W.E. Conrad, C.A. Vanderwerf, *J. Am. Chem. Soc.*, **1952**, 74, 1168–1171; (b) A.I. Moskalenko, V. I. Boev, *Russ. J. Org. Chem.*, **2010**, 46, 602–604; (c) P.T. Lansbury, N.R. Mancuso, *J. Am. Chem. Soc.*, **1966**, 88, 1205–1212; (d) R. Huisgen, *Justus Liebigs Ann. Chem.*, **1951**, 574, 171–184; (e) W.H. Pearson, B.M. Gallagher, Tetrahedron, **1996**, 52, 12039–12048; (f) R. Fusco, S. Rossi, *Gazzett*, **1959**, 81, 475; (g) A. Wrobleski, K. Sahasrabudhe, J. Aube, *J. Am. Chem. Soc.*, **2004**, 126, 5475–5481.
[16] (a) G.I. Koldobskii, V.A. Ostrovskii, B.V. Gidaspov, *Khim. Geterotsikl. Soedin.*, **1975**, 6, 723–735; (b) G.R. Krow, *Tetrahedron*, **1981**, 37, 1283–1307; (c) W.H. Pearson, *J. Heterocycl. Chem.*, **1996**, 33, 1489–1496; (d) W.R. Judd, C.E. Katz, J. Aube, *Sci. Synth.*, **2005**, 21, 133–178; (e) S. Braese, C. Gil, K. Knepper, V. Zimmermann, *Angew. Chem. Int. Ed.*, **2005**, 44, 5188–5240.

[17] (a) R. Iyengar, K. Schidknegt, M. Morton, J. Aube, *J. Org. Chem.*, **2005**, 70, 10645–10652; (b) G.F. Alberici, J. Andrieux, G. Adam, M.M. Plat, *Tetrhedron Lett.*, **1983**, 24, 1937–1940; (c) P.E. Eaton, R.E. Hormann, *J. Am. Chem. Soc.*, **1987**, 109, 1268–1269; (d) S. Furmeier, J.O. Metzger, *Eur. J. Org. Chem.*, **2003**, 2003, 885–893; (e) J.E. Golden, J. Aubé, *Angew. Chem. Int. Ed.*, **2002**, 41, 4316–4318; (f) M. Mascal, C.J. Moody, *J. Chem. Soc. Chem. Commun.*, **1988**, 589–590.
[18] (a) Y. Misaka, T. Mizutani, M. Sekido, S. Uyeo, *J. Chem. Soc. Chem. Commun.*, **1967**, 1258–1259; (b) G. Vidari, M. Tripolini, P. Novella, P. Allegrucci, L. Garlaschelli, *Tetrahedron: Asymmetry*, **1997**, 8, 2893–2903; (c) W.H. Pearson, W.K. Fang, *J. Org. Chem.*, **2000**, 65, 7158–7174; (d) B.T. Smith, J.A. Wendt, J. Aube, *Org. Lett.*, **2002**, 4, 2577–2579; (e) H.J. Cristau, X. Marat, J.P. Vors, J.L. Pirat, *Tetrahedron Lett.*, **2003**, 44, 3179–3181.
[19] (a) E. Nyfeler, P. Renaud, *Chimia Int. J. Chem.*, **2006**, 60, 276–284; (b) N. Doorenbos, M. Wu, *J. Org. Chem.*, **1961**, 26, 2548–2549; (c) M. Kawase, *J. Chem. Soc.*, **1992**, 1076–1077; (d) M.S. Ahmad, N.K. Pillai, *Aust. J. Chem.*, **1973**, 26, 603–607.
[20] (a) S. Mor, P. Pahal, *Der Pharma Chemica*, **2015**, 7(8), 118–129; (b) S. Mor, P. Pahal, Chemistry & Biology Interface, **2016**, 6, 198–209; (c) N. Devi, D. Singh, Honey, S. Mor, S. Chaudhary, R. K. Rawal, V. Kumar, A. K. Chowdhury, V. Singh, *RSC Adv.*, **2016**, 6, 43881–43891.
[21] T.M. Al-Nakib, T. Lorand, A. Foldesi, R. Varghese, *Med. Princ. Pract.*, **2001**, 10, 191–196.
[22] T.M. Al-Nakib, P. Perjesi, R. Varghese, M.J. Meegan, *Med. Princ. Pract.*, **1997**, 6, 14–21.
[23] D. Basavaiah, R.M. Reddy, *Tetrahedron Lett.*, **2001**, 42, 3025–3027.
[24] G. Tarczay, K. Vekey, K. Ludanyi, P. Perjesi, P. Sohar, *J. Mol. Struct.*, **2000**, 520, 97–102.
[25] G.A. Coppens, M. Coppens, D.N. Keville, N.H. Cromwell, *J. Org. Chem.*, **1963**, 28, 3267–3269.
[26] R. Bansal, G. Narang, C. Zimmer, R.W. Hartmann, *Med. Chem. Res.*, **2011**, 20, 661–669.
[27] A.P. Acharya, R.D. Kamble, S.D. Patil, S.V. Hese, O.S. Yemul, S.G. Patil, S.N. Halale, B.S. Dawane, *Chemical Papers*, **2014**, 68, 719–724.
[28] J.L. Imbach, A.E. Pohland, E.D. Weiler, N.H. Cromwell, *Tetrahedron*, **1967**, 23, 3931–3941.
[29] C.G. Lee, K.Y. Lee, S. Lee, J.N. Kim, *Tetrahedron*, **2005**, 61, 1493–1499.
[30] C. Dengiz, M. Balci, *Turk. J. Chem.*, **2013**, 37, 220–227.
[31] W.F. Wang, J. Fan, C.Z. Luo, Y.F. Yuan, Y.F. Zhang, *Arkivoc*, **2011**, xi, 105–120.
[32] M.M. Blanco, M.S. Shmidt, I.A. Perillo, *Arkivoc*, **2009**, xii, 106–118.
[33] R. Pathak, S. Madapa, S. Batra, *Tetrahedron*, **2007**, 63, 451–460.