PART-A

CHAPTER-5

EXPERIMENTAL
General Experimental section

All chemicals, reagents and solvents were of commercially high purity grade purchased from Avra Synthesis Pvt. Ltd. and Merck Ltd. India. Silica gel (60-120 mesh) was used for column chromatographic isolation and purification of the amides synthesized. Organic azides used in the investigation were prepared according to the literature procedures. Melting points were obtained on electro-thermal apparatus and are uncorrected. $^1$H NMR and $^{13}$C NMR spectra were recorded in CDCl$_3$ on Bruker Avance 300 MHz spectrometer and the chemical shifts are reported as $\delta$ values in parts per million (ppm) relative to tetramethylsilane, with $J$ values in Hertz. The splitting patterns in $^1$H NMR spectra are reported as follows: s = singlet; d = doublet; t = triplet; q = quartet; br s = broad singlet; br d = broad doublet; m = multiplet. $^{13}$C NMR data are reported with the solvent peak (CDCl$_3$ = 77.0) as the internal standard. Elemental analyses were performed by C.N.R.S-Vernaison, and were in agreement with the calculated values within ±0.4%.

CHAPTER-2

“Solvent-free Aza-wittig protocol for amide bond formation via trapping of nascent phosphazenes with carboxylic acids”

Experimental procedure for the preparation of azides (2a-d) used in the synthesis of amides (3):

1. Benzyl azide (2a)$^1$: To a stirred solution of the benzyl bromide (1g, 5.84 mmol) in water/acetone mixture (1:4 v/v, 10 ml), sodium azide (0.57 g, 8.77 mmol) was added. The resulting suspension was stirred at room temperature for 24 hours. Dichlormethane was added to the mixture and the organic layer was separated. The aqueous layer was extracted with dichlormethane (3 x 10 ml) and the combined organic layers were dried over anhydrous magnesium sulphate. Solvent was removed under reduced pressure, and the azide was obtained in quantitative yield sufficiently pure to use without further work up.
2. 1-Azido-3-phenyl-2-cyclohex-2-ene (2b): To 20% ethanolic potassium hydroxide (10 ml), 1a-azido-2a-iodo-1e-phenylcyclohexane (1.0 g, 3.0 mmol) was added and the mixture refluxed for 1 hour in water bath. Then the mixture after cooling to room temperature was added to excess water and extracted with ether (3 x 20 ml). The organic extract was washed repeatedly with water, dried over anhydrous magnesium sulphate to give the allyl azide (2b) contaminated with 1-phenylcyclohexene. Column chromatographic purification on silica with pet ether/ethyl acetate as the eluant afford 1-azido-3-phenyl-2-cyclohex-2-ene (2b) in good yield.

3. Azidobenzene (2c) & 1-Azido-4-bromobenzene (2d): These azides were prepared by the diazotization procedure similar to that used for the preparation of iodobenzene from aminobenzene by diazotization followed by treatment of aqueous potassium iodide at low temperature. Herein, by the same procedure diazotized solution of aminobenzene and 1-amino-4-bromobenzene were treated with aqueous sodium azide to afford the corresponding organic azides (2c) and (2d) respectively which were used without further purification for the synthesis of amides in our investigation.

General procedure for micro-wave accelerated synthesis (MAS)/Glycerol Bath accelerated synthesis (GBAS) of amides (3)

To a well ground intimate mixture of triphenylphosphine (1.1 mmol) and the carboxylic acid, (1, 1.0 mmol), the organic azide,18 (2a, 1.0 mmol) was added in drops while stirring. Stirring continued until liberation of nitrogen ceased and the mixture irradiated with micro-wave (180°C) or preheated glycerol bath at 180-190°C for 15 minutes. The residue purified by column chromatography on silica (pet ether/ethyl acetate) afford the amide, (3) as solid in very good yield.

1. N-(3-Phenylcyclohex-2-enyl)acetamide (3a)

Yield: 81%; white solid, mp: 118 °C; IR (KBr) νmax: 3445 (-NH), 1671 (-C=O); 1H NMR (300 MHz, CDCl3) δ (ppm): 7.20-7.40 (m, 5H, ArH), 5.96 (pseudo triplet, 1H, C=CH), 5.60 (br d, 1H, J= 7.5 Hz, -NH), 4.70 (br s, 1H, CHN), 1.99 (s, 3H, -COCH3), 2.20-2.42 (m, 2H, Alicyclic protons), 1.95-2.07 (m, 1H, Alicyclic proton), 1.65-1.77
PART A Experimental

(m, 2H, Alicyclic protons), 1.39-1.53 (m, 1H, Alicyclic proton). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ (ppm): 169.48, 148.11, 139.99, 138.72, 126.21, 125.00, 123.69, 45.51, 29.03, 27.10, 23.27, 20.18. Anal.cald (%) C$_{14}$H$_{17}$NO: C, 78.10; H, 7.96; N, 6.51. Found (%) C, 78.25; H, 7.95; N, 6.51.

2. N-(3-Phenylcyclohex-2-enyl)propionamide (3b)

![Structure of 3b]

Yield: 83%; white solid, mp: 97 ºC; IR (KBr) $\nu_{max}$: 3444 (-NH), 1682 (-C=O); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ (ppm): 7.20-7.50 (m, 5H, ArH), 5.96 (br s, 1H, C=CH), 5.62 (br d, 1H, J= 6.9 Hz, -NH), 4.70 (br s, 1H, CHN), 2.21 (q, 2H, J= 7.5 Hz, COCH$_2$) 1.16 (t, 3H, J= 7.5 Hz, -CH$_3$), 2.20-2.42 (m, 2H, Alicyclic protons), 1.95-2.07 (m, 1H, Alicyclic proton), 1.65-1.77 (m, 2H, Alicyclic protons), 1.39-1.53 (m, 1H, Alicyclic proton). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ (ppm): 173.03, 141.21, 140.19, 128.27, 127.36, 125.14, 124.62, 45.32, 29.84, 29.12, 27.16, 20.32, 9.88. Anal.cald (%) C$_{15}$H$_{18}$NO: C, 78.56; H, 8.35; N, 6.11. Found (%) C, 78.46; H, 8.36; N, 6.10.

3. 2-Phenyl-N-(3-phenylcyclohex-2-enyl)acetamide (3c)

![Structure of 3c]

Yield: 80%; white solid, mp: 77 ºC; IR (KBr) $\nu_{max}$: 3451 (-NH), 1670 (-C=O); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ (ppm): 7.20-7.45 (m, 10H, ArH), 5.85 (br s, 1H, C=CH), 5.50 (br d, 1H, J= 7.6 Hz, -NH), 4.72 (br s, 1H, CHN), 3.63 (s, 2H, -COCH$_2$), 2.20-2.42 (m, 2H, Alicyclic protons), 1.95-2.07 (m, 1H, Alicyclic proton), 1.65-1.77 (m, 2H, Alicyclic protons), 1.39-1.53 (m, 1H, Alicyclic proton). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 170.39, 141.11, 140.39, 134.79, 129.30, 129.37, 129.01, 128.30, 127.33, 125.15, 124.23, 45.77, 43.93, 29.03, 27.11, 20.35. Anal.cald (%) C$_{20}$H$_{21}$NO: C, 82.44; H, 7.26; N, 4.81. Found (%) C, 82, 56; H, 7.26; N, 4.81.
4. 2-Phenoxy-N-(3-phenylcyclohex-2-enyl)acetamide (3d)

Yield: 78% white solid, mp: 107 ºC; IR (KBr) $\nu_{\text{max}}$: 3450 (-NH), 1674 (-C=O); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ (ppm): 7.02-7.41 (m, 10H, ArH), 5.97 (br s, 1H, C=CH), 6.63 (br d, 1H, J= 7.8 Hz,-NH), 4.82 (br s, 1H, CHN), 4.52 (s, 2H, COCH$_2$), 2.20-2.42 (m, 2H, Alicyclic protons), 1.95-2.07 (m, 1H, Alicyclic proton), 1.65-1.77 (m, 2H, Alicyclic protons), 1.39-1.53 (m, 1H, Alicyclic proton). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ (ppm): 167.51, 157.11, 140.72, 129.73, 128.34, 127.54, 125.19, 123.97, 122.07, 114.66, 67.32, 45.27, 29.07, 27.12, 20.37. Anal.cald (%) C$_{20}$H$_{21}$NO$_2$: C, 78.15; H, .89; N, 4.56. Found (%) C, 78.35; H, 6.90; N, 4.55.

5. N-(3-Phenylcyclohex-2-enyl)benzamide (3e)

Yield: 82%; white solid, mp : 154 ºC; IR (KBr) $\nu_{\text{max}}$: 3447 (-NH), 1680 (-C=O); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ (ppm): 7.29-7.75 (10H, m, ArH), 6.00 (br s, 1H, C=CH), 5.60 (br d, 1H, J= 8.4 Hz, NH), 4.60 (br s, 1H, CHN), 2.20-2.42 (m, 2H, Alicyclic protons), 1.95-2.07 (m, 1H, Alicyclic proton), 1.65-1.77 (m, 2H, Alicyclic protons), 1.39-1.53 (m, 1H, Alicyclic proton). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ (ppm): 166.79, 148.27, 140.40, 138.61, 134.70, 131.31, 128.45, 126.91, 126.41, 125.18, 123.61, 45.06, 29.19, 27.27, 20.42. Anal.cald (%) C$_{19}$H$_{19}$NO: C, 82.28; H, 6.90; N, 4.05. Found (%) C, 82.13; H, 6.91; N, 5.06.

6. 2-Chloro-N-(3-phenylcyclohex-2-enyl)benzamide (3f)

Yield: 78%; white solid, mp : 122 ºC; IR (KBr) $\nu_{\text{max}}$: 3454 (-NH), 1678 (-C=O); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ (ppm): 7.25-7.95 (m, 9H, ArH), 6.07 (br s, 1H, C=CH), 6.23
(br d, 1H, J= 8.4 Hz, -NH), 4.92 (br s, 1H, CHN), 2.20-2.42 (m, 2H, Alicyclic protons), 1.95-2.07 (m, 1H, Alicyclic proton), 1.65-1.77 (m, 2H, Alicyclic protons), 1.39-1.53 (m, 1H, Alicyclic proton). ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 165.80, 141.20, 140.32, 135.24, 131.20, 130.56, 130.16, 128.34, 127.51, 127.09, 125.28, 123.86, 46.23, 28.98, 27.27, 20.27. Anal.cald (%) C₁₉H₁₈ClNO: C, 73.19; H, 5.82; N, 4.49. Found (%) C, 73.29; H, 5.82; N, 4.49.

7. 2-Bromo-N-(3-phenylcyclohex-2-enyl)benzamide (3g)

Yield: 75%; white solid, mp: 119ºC; IR (KBr) νmax: 3457 (-NH), 1684 (-C=O); ¹H NMR (300 MHz, CDCl₃) δ (ppm): 7.07-7.75 (m, 9H, ArH), 5.97 (br s, 1H, C=C H), 6.55 (br d, 1H, J= 8.0 Hz, -NH), 4.80 (br s, 1H, CHN), 2.20-2.42 (m, 2H, Alicyclic protons), 1.95-2.07 (m, 1H, Alicyclic proton), 1.65-1.77 (m, 2H, Alicyclic protons), 1.39-1.53 (m, 1H, Alicyclic proton). ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 166.88, 141.16, 140.93, 137.85, 133.24, 131.14, 129.52, 128.31, 127.53, 127.48, 125.24, 123.72, 119.17, 46.15, 28.87, 27.23, 20.22. Anal.cald (%) C₁₉H₁₈BrNO: C, 64.06; H, 5.09; N, 3.93. Found (%) C, 64.18; H, 5.10; N, 3.93.

8. 4-Chloro-N-(3-phenylcyclohex-2-enyl)benzamide (3h)

Yield: 84%; white solid, mp: 155ºC; IR (KBr) νmax: 3453 (-NH), 1684 (-C=O); ¹H NMR (300 MHz, CDCl₃) δ (ppm): 7.26-7.74 (9H, m, ArH), 6.06 (br s, 1H, C=CH), 6.22 (br d, 1H, J= 8.4 Hz, -NH), 4.91 (br s, 1H, CHN), 2.20-2.42 (m, 2H, Alicyclic protons), 1.95-2.07 (m, 1H, Alicyclic proton), 1.65-1.77 (m, 2H, Alicyclic protons), 1.39-1.53 (m, 1H, Alicyclic proton). ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 166.78, 141.16, 140.70, 134.67, 131.41, 128.54, 128.35, 127.50, 126.90, 125.22, 124.36, 45.98, 29.18, 27.62, 20.38. Anal.cald (%) C₁₉H₁₈ClNO: C, 73.19; H, 5.82; N, 4.49. Found (%) C, 73.26; H, 5.82; N, 4.50.
9. 4-Bromo-N-(3-phenylcyclohex-2-enyl)benzamide (3i)

Yield: 81%; white solid, mp: 163°C; IR (KBr) \( \nu_{\text{max}} \): 3449 (-NH), 1677 (-C=O); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \) (ppm): 7.20-7.72 (m, 9H, ArH), 6.04 (br s, 1H, C=CH), 6.13 (br d, 1H, J= 8.2 Hz, -NH), 4.85 (br s,1H, CHN), 2.20-2.42 (m, 2H, alicyclic protons), 1.95-2.07 (m,1H, Alicyclic proton), 1.65-1.77 (m, 2H, Alicyclic protons), 1.39-1.53 (m, 1H, Alicyclic proton). \(^1\)\(^3\)C NMR (75 MHz, CDCl\(_3\)) \( \delta \) (ppm): 164.34, 141.8, 137.74, 136.75, 135.73, 134.32, 129.78, 128.31, 128.29, 127.28, 124.32, 44.17, 28.35, 27.28, 20.48. Anal.cald (%) C\(_{19}\)H\(_{18}\)NOBr: C, 64.06; H, 5.09; N, 3.93. Found (%) C, 64.19; H, 5.08; N, 3.93.

10. 4-Methoxy-N-(3-phenylcyclohex-2-enyl)benzamide (3j)

Yield: 88%; white solid, mp: 172 °C; IR (KBr) \( \nu_{\text{max}} \): 3456 (-NH), 1675 (-C=O); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \) (ppm): 6.89-7.76 (m, 9H, ArH), 6.07 (br s, 1H, C=CH), 6.21 (br d, 1H, J= 7.8 Hz, -NH), 4.90 (br s, 1H, CHN), 3.85 (s, 3H, OCH\(_3\)), 2.20-2.42 (m, 2H, Alicyclic protons), 1.95-2.07 (m, 1H, Alicyclic proton), 1.65-1.77 (m, 2H, Alicyclic protons), 1.39-1.53 (m, 1H, Alicyclic proton). \(^1\)\(^3\)C NMR (75 MHz, CDCl\(_3\)) \( \delta \) (ppm): 166.26, 162.06, 141.18, 140.47, 128.68, 128.31, 127.43, 126.90, 125.18, 124.58, 113.65, 55.35, 45.88, 28.22, 27.23, 20.39. Anal.cald (%) C\(_{20}\)H\(_{21}\)NO\(_2\): C, 78.15; H, 6.89; N, 4.56. Found (%) C, 78.30; H, 6.88; N, 4.59.

11. 4-Nitro-N-(3-phenylcyclohex-2-enyl)benzamide (3k)

Yield: 67%; white solid, mp: 232 °C; IR (KBr) \( \nu_{\text{max}} \): 3452 (-NH), 1685 (-C=O); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \) (ppm): 7.26-7.74 (m, 9H, ArH), 6.10(br s, 1H, C=CH), 6.14 (br d, 1H, J= 8.2 Hz, -NH), 4.85 (br s, 1H, CHN), 2.20-2.42 (m, 2H, alicyclic protons), 1.95-2.07 (m,1H, Alicyclic proton), 1.65-1.77 (m, 2H, Alicyclic protons), 1.39-1.53 (m, 1H, Alicyclic proton). \(^1\)\(^3\)C NMR (75 MHz, CDCl\(_3\)) \( \delta \) (ppm): 165.86, 141.18, 139.75, 137.08, 135.73, 134.32, 129.78, 128.31, 128.29, 127.43, 126.90, 125.18, 124.58, 113.65, 55.35, 45.88, 28.22, 27.23, 20.39. Anal.cald (%) C\(_{19}\)H\(_{17}\)NO\(_2\): C, 78.15; H, 6.89; N, 4.56. Found (%) C, 78.30; H, 6.88; N, 4.59.
1H, J= 8.4 Hz, -NH), 4.89 (br s, 1H, CHN), 2.20-2.42 (m, 2H, Alicyclic protons), 1.95-2.07 (m, 1H, Alicyclic proton), 1.65-1.77 (m, 2H, Alicyclic protons), 1.39-1.53 (m, 1H, Alicyclic proton). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ (ppm): 168.21, 153.12, 142.38, 141.52, 140.39, 139.47, 128.27, 127.36, 126.05, 126.72, 117.65, 45.32, 29.32, 27.07, 20.11. Anal.cald (%) C$_{19}$H$_{18}$N$_2$O$_3$: C, 70.79; H, 5.63; N, 8.69. Found (%) C, 70.69; H, 5.63; N, 8.68.

12. N-(3-Phenylcyclohex-2-enyl)furan-2-carboxamide (3l)

Yield: 79%; white solid, mp: 70 ºC; IR (KBr) $\nu_{\text{max}}$: 3446 (-NH), 1674 (-C=O); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ (ppm): 7.20-7.60 (m, 5H, ArH), 6.40-6.60 (m, 3H, heteroaromatic protons), 6.05 (br s, 1H, C=CH), 5.92 (br d, 1H, J= 8.4 Hz, -NH), 4.85 (br s, 1H, CHN), 2.20-2.42 (m, 2H, Alicyclic protons), 1.95-2.07 (m, 1H, Alicyclic proton), 1.65-1.77 (m, 2H, Alicyclic protons), 1.39-1.53 (m, 1H, Alicyclic proton). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ (ppm): 162.30, 157.7, 147.78, 143.87, 141.11, 128.32, 127.49, 125.21, 124.00, 114.54, 112.21, 45.29, 29.13, 27.18, 20.28. Anal.cald (%) C$_{17}$H$_{17}$NO$_2$: C, 76.38; H, 6.41; N, 5.24. Found (%) C, 76.48; H, 6.40; N, 5.25.

13. N-(3-Phenylcyclohex-2-enyl)cinnamamide (3m)

Yield: 75%; white solid, mp: 147 ºC; IR (KBr) $\nu_{\text{max}}$: 3448 (-NH), 1672 (-C=O); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ (ppm): 7.25-7.50 (m, 10H, ArH), 7.63 (d, 1H, J= 14.4 Hz, -C=CH), 6.40 (d, 1H, J= 14.4 Hz, -C=CH), 6.03 (br s, 1H, C=CH), 5.92 (br d, 1H, J= 7.5 Hz, -NH), 4.84 (br s, 1H, CHN), 2.20-2.42 (m, 2H, Alicyclic protons), 1.95-2.07 (m, 1H, Alicyclic proton), 1.65-1.77 (m, 2H, Alicyclic protons), 1.39-1.53 (m, 1H, Alicyclic proton). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ (ppm): 165.14, 141.15, 140.98, 140.42, 135.21, 129.58, 128.75, 128.30, 127.73, 127.42, 125.17, 124.33, 120.80, 45.63, 29.12, 27.17, 20.28.
Anal.cald (%) C\textsubscript{21}H\textsubscript{21}NO: C, 83.13; H, 6.98; N, 4.62. Found (%) C, 83.29; H, 6.97; N, 4.62.

14. (E)-N-(3-Phenylcyclohex-2-enyl)-3-(3,4,5-trimethoxyphenyl)-acrylamide (3n)

Yield: 70%; white solid, mp: 137 °C; IR (KBr) \( \delta_{\text{max}} \): 3450 (-NH), 1674 (-C=O); \(^1\)H NMR (300 MHz, CDCl\textsubscript{3}) \( \delta \) (ppm): 7.21-7.59 (m, 7H, ArH), 7.65 (d, 1H, J= 14.6 Hz -C=CH), 6.42 (d, 1H, 14.6 Hz -C=CH), 6.01 (br s, 1H, C=CH), 5.90 (br d, 1H, J= 7.5 Hz, -NH), 4.81 (br s, 1H, CHN), 3.94 (s, 9H, -(OCH\textsubscript{3})\textsubscript{3}) 2.20-2.42 (m, 2H, Alicyclic protons), 1.95-2.07 (m, 1H, Alicyclic proton), 1.65-1.77 (m, 2H, Alicyclic protons), 1.39-1.53 (m, 1H, Alicyclic proton). \(^1\)C NMR (75 MHz, CDCl\textsubscript{3}) \( \delta \) (ppm): 171.33, 153.21, 149.32, 144.21, 142.31, 141.31, 138.27, 128.72, 128.69, 127.34, 126.40, 124.71, 123.52, 62.72, 58.37, 45.21, 28.11, 27.07, 20.09. Anal.cald (%) C\textsubscript{24}H\textsubscript{27}NO\textsubscript{4}: C, 73.26; H, 6.92; N, 3.56. Found (%) C, 73.35; H, 6.92; N, 3.56.
CHAPTER 3

“An environmentally benign solvent/catalyst-free one-pot synthesis of N-substituted phthalimides via Aza-wittig reaction”

General procedure for the synthesis of N-substituted phthalimides
To a well ground intimate mixture of triphenyl phosphine (1 mmol) and phthalic anhydride, (1 mmol) in a microwave vial (10 mL) equipped with a magnetic stirring bar, organic azide (1 mmol) was added in drops while stirring. Stirring was continued until liberation of nitrogen ceased and the reaction vessel was heated to 120°C for 30 minutes. The reaction vessel was then cooled to room temperature and the residue subjected to column chromatography to get the pure product.

1. 2-Benzylisoindoline-1,3-dione (2a)

Yield: 84%; white solid, mp: 118-120 °C; $^1$H NMR (300 MHz, CDCl$_3$) δ (ppm): 7.78 (m, 2H, ArH), 7.62 (m, 2H, ArH), 7.36 (m, 2H, ArH), 7.26 (m, 3H, ArH), 4.78 (s, 2H, CH$_2$).

2. Ethyl 2-(1,3-dioxoisindolin-2-yl)acetate (2b)

Yield: 81%; white solid, mp: 111-112 °C; $^1$H NMR (300 MHz, CDCl$_3$) δ (ppm): 7.88 (m, 2H, ArH), 7.74 (m, 2H, ArH), 4.56 (s, 2H, CH$_2$), 4.23 (q, 2H, J= 7.2 Hz, CH$_2$), 1.28 (t, 3H, J= 7.2 Hz, CH$_3$).

3. Methyl 2-(1,3-dioxoisindolin-2-yl)acetate (2c)
PART A Experimental

Yield: 79%; white solid, mp: 114-115 °C; $^1$H NMR (300 MHz, CDCl$_3$) δ (ppm): 7.95-7.84 (m, 2H, ArH), 7.79-7.71 (m, 2H, ArH), 4.45 (s, 2H, CH$_2$), 3.77 (s, 3H, CH$_3$).

4. 2-(2-Oxo-2-phenylethyl)isoindole-1,3-dione (2d)$^7$

Yield: 82%; white solid, mp: 160-162 °C; $^1$H NMR (300 MHz, CDCl$_3$) δ (ppm): 8.03 (m, 2H, ArH), 7.91 (m, 2H, ArH), 7.75 (m, 2H, ArH), 7.52-7.64 (m, 3H, ArH), 5.13 (s, 2H, CH$_2$).

5. 2-Tosylisoindole-1,3-dione (2e)$^8$

Yield: 80%; white solid, mp: 240-241 °C; $^1$H NMR (300 MHz, CDCl$_3$) δ (ppm) 7.95 (m, 2H, ArH), 7.77 (m, 2H, ArH), 7.26-7.39 (m, 4H, ArH), 2.41 (s, 3H, CH$_3$).

6. 2-Phenylisoindole-1,3-dione (2f)$^9$

Yield: 75%; white solid, mp: 209-210 °C; $^1$H NMR (300 MHz, CDCl$_3$) δ (ppm): 7.97 (m, 2H, ArH), 7.79-7.82 (m, 2H, ArH), 7.50-7.54 (m, 2H, ArH), 7.40-7.46 (m, 3H, ArH).

7. 2-(4-Bromophenyl)isoindole-1,3-dione (2g)$^9$

Yield: 78%; white solid, mp: 191-192 °C; $^1$H NMR (300 MHz, CDCl$_3$) δ (ppm): 7.98 (m, 2H, ArH), 7.80-7.81 (m, 2H, ArH), 7.62-7.66 (m, 2H, ArH), 7.34-7.38 (m, 2H, ArH).
8. 2-p-Tolylisoindoline-1,3-dione (2h)\(^9\)

\[
\text{Yield: 83\%; white solid, mp: 203-205}^\circ \text{C; } ^1\text{H NMR (300 MHz, CDCl}_3\text{)} \delta (\text{ppm}): 7.94-7.95 (m, 2H, ArH), 7.77-7.80 (m, 2H, ArH), 7.31 (m, 4H, ArH), 2.41 (s, 3H, CH}_3\text{).}
\]

**CHAPTER 4**

“Microwave-assisted clean synthesis of amides via solvent-free Aza-wittig reaction”

**General procedure for the synthesis of amides**

To an intimate mixture of triethylphosphite (1 mmol) and organic azide (1 mmol) in a micro-wave vial (10 mL) equipped with a magnetic stirring bar, acid anhydride/acid chloride (1.3 mmol) was added in drops while stirring. Stirring was continued until liberation of nitrogen ceased and the reaction vessel was sealed with a septum. It was then placed into the cavity of a focused monomode micro-wave reactor (CEM Discover, benchmate) and operated for 15 minutes at 150\(^\circ\)C (temperature monitored by a built-in IR sensor). The reaction vessel was then cooled to room temperature and the residue was dissolved in ethylacetate and washed repeatedly with water followed by saturated sodium bicarbonate solution to afford the amide as white solid.

1. **N-Benzylacetamide (1a)\(^10\)**

\[
\text{Yield: 74\%; white solid, mp: 58}^\circ \text{C; } ^1\text{H NMR (300 MHz, CDCl}_3\text{)} \delta (\text{ppm}): 7.33-7.36 (m, 5H, ArH), 5.10 (s, 2H, CH}_2\text{N), 2.09 (s, 3H, CH}_3\text{).}
\]
2. N-Benzylpropionamide (1b)\textsuperscript{11}

\[
\begin{array}{c}
&\text{O} \\
&\text{H} \\
&\text{N} \\
&\text{H}
\end{array}
\]

Yield: 78%; white solid, mp: 47 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)) δ (ppm): 7.12-7.33 (m, 5H, ArH), 4.99 (s, 2H, CH\(_2\)), 2.75 (q, 2H, J= 7.2 Hz, CH\(_2\)), 1.14 (t, 3H, J= 7.2 Hz, CH\(_3\)).

3. N-Benzylbutyramide (1c)\textsuperscript{12}

\[
\begin{array}{c}
&\text{O} \\
&\text{H} \\
&\text{N} \\
&\text{H}
\end{array}
\]

Yield: 84%; Viscous liquid; \(^1\)H NMR (300 MHz, CDCl\(_3\)) δ (ppm): 7.12-7.35 (m, 5H, ArH), 4.98 (s, 2H, CH\(_2\)-N), 2.69 (t, 2H, J= 7.2 Hz, CH\(_2\)), 1.69 (sextet, 2H, J= 7.2 Hz, CH\(_2\)), 0.93 (t, 3H, J= 7.2 Hz, CH\(_3\)).

4. N-Benzylbenzamide (1d)\textsuperscript{11}

\[
\begin{array}{c}
&\text{O} \\
&\text{H} \\
&\text{N} \\
&\text{H}
\end{array}
\]

Yield: 76%; white solid, mp: 103 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)) δ (ppm): 7.32-8.18 (m, 10H, ArH), 6.61 (br s, 1H, NH), 4.65 (d, 2H, J= 5.7 Hz, CH\(_2\)-N).

5. N-Phenylacetamide (2a)\textsuperscript{13}

\[
\begin{array}{c}
&\text{O} \\
&\text{H} \\
&\text{N} \\
&\text{H}
\end{array}
\]

Yield: 75%; white solid, mp: 115 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)) δ (ppm): 7.08-7.50 (m, 5H, ArH), 2.18 (s, 3H, CH\(_3\)).

6. N-Phenylpropionamide (2b)\textsuperscript{13}

\[
\begin{array}{c}
&\text{O} \\
&\text{H} \\
&\text{N} \\
&\text{H}
\end{array}
\]

Yield: 80%; white solid, mp: 105 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)) δ (ppm): 7.06-7.56 (m, 5H, ArH), 2.38 (q, 2H, J= 7.5 Hz, CH\(_2\)), 1.24 (t, 3H, J= 7.5 Hz, CH\(_3\)).
7. N-Phenylbutyramide (2c)\(^{12}\)

![N-Phenylbutyramide (2c)](image)

Yield: 83%; viscous liquid; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) (ppm): 7.06-7.52 (m, 5H, ArH), 2.32 (t, 2H, J= 7.5 Hz, CH\(_2\)), 1.75 (sextet, 2H, J= 7.5 Hz, CH\(_2\)), 0.99 (t, 3H, J= 7.5 Hz, CH\(_3\)).

8. N-Phenylbenzamide (2d)\(^{11}\)

![N-Phenylbenzamide (2d)](image)

Yield: 77%; white solid, mp: 164 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) (ppm): 7.62-7.58 (m, 6H, ArH).

9. N-(3-Phenylcyclohex-2-enyl)acetamide (3a)

![N-(3-Phenylcyclohex-2-enyl)acetamide (3a)](image)

Yield: 81%; white solid; mp: 118 °C; IR (KBr) \(\nu_{\text{max}}\): 3445 (-NH), 1671 (-C=O); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) (ppm): 7.20-7.40 (m, 5H, ArH), 5.96 (pseudo triplet, 1H, C=CH), 5.60 (br d, 1H, J= 7.5 Hz, -NH), 4.70 (br s,1H, CHN), 1.99 (s, 3H, -COCH\(_3\)), 2.20-2.42 (m, 2H, Alicyclic protons), 1.95-2.07 (m, 1H, Alicyclic proton), 1.65-1.77 (m, 2H, Alicyclic protons), 1.39-1.53 (m, 1H, Alicyclic proton). \(^13\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) (ppm): 169.4, 148.1, 139.9, 138.7, 126.2, 125.0, 123.6, 45.5, 29.0, 27.1, 23.2, 20.1. Anal.cald (%) for C\(_{14}\)H\(_{17}\)NO: C, 78.10; H, 7.96; N, 6.51. Found (%) C, 78.25; H, 7.95; N, 6.51.

10. N-(3-Phenylcyclohex-2-enyl)propionamide (3b)

![N-(3-Phenylcyclohex-2-enyl)propionamide (3b)](image)

Yield 85%; white solid, mp: 97 °C; IR (KBr) \(\nu_{\text{max}}\): 3444 (-NH), 1682 (-C=O); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) (ppm): 7.20-7.50 (m, 5H, ArH), 5.96 (pseudo triplet, 1H, C=CH), 5.62 (br d, 1H, J= 6.9 Hz, -NH), 4.70 (br s, 1H, CHN), 2.21 (q, 2H, J= 7.5 Hz, COCH\(_2\))
1.16 (t, 3H, J= 7.5 Hz, CH₃), 2.20-2.42 (m, 2H, Alicyclic protons), 1.95-2.07 (m, 1H, Alicyclic proton), 1.65-1.77 (m, 2H, Alicyclic protons), 1.39-1.53 (m, 1H, Alicyclic proton). ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 173.0, 141.2, 140.1, 128.2, 127.3, 125.1, 124.6, 45.3, 29.8, 29.1, 27.1, 20.3, 9.8. Anal.cald (%) C₁₅H₁₉NO: C, 78.56; H, 8.35; N, 6.11. Found (%) C, 78.46; H, 8.36; N, 6.10.

11. N-(3-Phenylcyclohex-2-enyl)butyramide (3c)

![Structure of N-(3-Phenylcyclohex-2-enyl)butyramide (3c)](image)

Yield: 88%; white solid, mp: 128-129 ºC; IR (KBr) v_max: 3447 (-NH), 1692 (-C=O); ¹H NMR (300 MHz, CDCl₃) δ (ppm): 7.25-7.39 (m, 5H, ArH), 5.96 (s, 1H, C=CH), 4.71 (br s, 1H, CHN), 2.36-2.40 (m, 2H), 2.16 (m, 2H), 1.95-1.97 (m, 1H, Alicyclic protons), 1.81-1.83 (m, 2H, Alicyclic protons), 1.68 (m, 2H, Alicyclic protons), 1.55-1.57 (m, 1H, Alicyclic protons), 0.95 (t, 3H, J= 14.7 Hz, CH₃). ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 172.9, 141.2, 140.2, 128.2, 127.3, 125.1, 124.6, 45.3, 29.8, 29.1, 27.2, 20.3, 18.3, 9.8. Anal.Cald (%) C₁₆H₂₁NO: C, 78.97; H, 8.70; N, 5.76. Found (%) C, 78.88; H, 8.72; N, 5.77.

12. N-(3-Phenylcyclohex-2-enyl)acetamide (3a)

![Structure of N-(3-Phenylcyclohex-2-enyl)acetamide (3a)](image)

Yield: 77% (with respect to acetyl chloride)

13. N-(3-Phenylcyclohex-2-enyl)benzamide (3d)

![Structure of N-(3-Phenylcyclohex-2-enyl)benzamide (3d)](image)

Yield: 79%; white solid, mp: 154 ºC; IR (KBr) v_max: 3451 (-NH), 1670 (-C=O); ¹H NMR (300 MHz, CDCl₃) δ (ppm): 7.29-7.75 (m, 10H, ArH), 6.00 (br s, 1H, C=CH), 5.60 (br d, 1H, J= 8.4 Hz, NH), 4.60 (br s, 1H, CHN), 2.20-2.42 (m, 2H, Alicyclic protons), 1.95-2.07 (m, 1H, Alicyclic proton), 1.65-1.77 (m, 2H, Alicyclic protons), 1.39-1.53 (m, 1H, Alicyclic proton). ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 166.7, 148.2, 140.4, 138.6,
134.7, 131.3, 128.4, 126.9, 126.4, 125.1, 123.6, 45.0, 29.1, 27.2, 20.4. Anal. calcd (%) 
C\textsubscript{19}H\textsubscript{19}NO: C, 82.28; H, 6.90; N, 4.05. Found (%) C, 82.13; H, 6.91; N, 5.06.

References:
1. L. S. Campbell-Verduyn, L. Mirfeizi, R. A. Dierckx, P. H. Elsinga and B. L. Feringa, 