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Original Research Article

1, 3, 8-Triaza- Cyclopenta[α] Indene: Compound with Potential Biological Activities

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ABSTRACT

Compound with potential biological activities viz. antimicrobial, anticonvulsant, anti-inflammatory and antitubercular etc. have been synthesized and their structure were established on the basis of elemental (C, H, N) and spectral (1H-NMR, 13C-NMR and spectral data) analysis.

Keywords: Titanium dioxide, ammonium acetate, 1-Phenyl- 1H- indole- 2, 3-dione, 2, 8-Diphenyl-1, 3a, 8, 8a-tetrahydro- 1, 3, 8-triaza- cyclopenta[α] indene, anticonvulsant, antidepressant, antitubercular, antidiabetic, anti-inflammatory, anthelmentic, antiallergic, antitumor, anti-HIV, antimicrobial, and anti-inflammatory.

INTRODUCTION

Indole derivatives have been found to posses potential biological activities such as anticonvulsant,[1] antidepressant,[2] anti-histamine, antitubercular,[3] cardio-vascular, antidiabetic,[4] anti-inflammatory,[5] anthelmentic and antiallergic. [6] Imidazole analogs deal with a variety of bioactivities viz. antitumor,[7,8] anti-HIV,[9] anti-microbial,[10] anticonvulsant, antitubercular, antiprotozoal, anti-inflammatory. [11]

METHOD

EXPERIMENTAL

GENERAL

All chemicals were used as received without further purification. NMR spectra were recorded on a Bruker Advance DPX-400400 FT spectrometer (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C) using $CDCl_3$ as solvent and TMS as an internal reference. Mass spectra were recorded on a JEOL SX-102 (FAB) mass spectrometer at 70 eV. Elemental analyses were carried out in a Coleman automatic carbon, hydrogen and nitrogen analyzer. Silica gel-G was used for TLC. Melting points were determined by open glass capillary method and are uncorrected.

Scheme: Synthesis of 2, 8-Diphenyl-1, 3a, 8, 8a-tetrahydro- 1, 3, 8-triaza-cyclopenta[α] indene

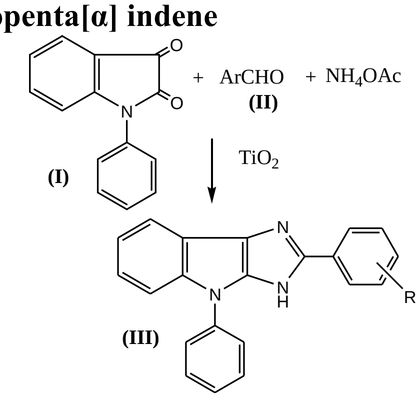
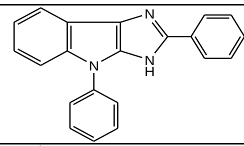
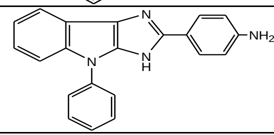
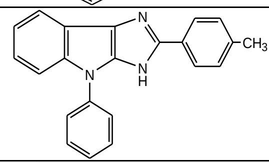
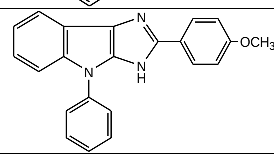
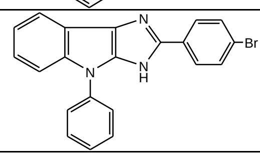
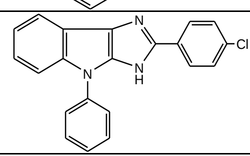


Table 1: Various derivatives of 2, 8-Diphenyl-1, 3a, 8, 8a-tetrahydro- 1, 3, 8-triaza- cyclopenta[α] indene, their product, reaction-time and yield

Entry	Ar	Product	Time(hrs)	Yield (%)
1.	C_6H_5		1.50	78
2.	4-H_2N-C_6H_4		1.70	82
3.	4-H_3C-C_6H_4		2.50	88
4.	4-H_3CO-C_6H_4		2.50	90
5.	4Br-C_6H_4		1.80	80
6.	4-Cl-C_6H_4		2.30	83

Synthesis of 2, 8-Diphenyl-1, 3a, 8, 8a-tetrahydro- 1, 3, 8-triaza- cyclopenta[α] indene (III):

Mixture of 1-Phenyl- 1H- indole- 2, 3-dione, I (1mmol), substituted aldehyde II (1mmol), ammonium acetate (4mmol) and titanium dioxide (4mmol) was heated at 120^{o}C in an oil-bath for a period of 1.50-2.50 hrs with continuous stirring using a bar magnet. The progress of the reaction was monitored by TLC. When reaction was completed then absolute ethanol was added and shaken well. The mass thus obtained was filtered to separate out titanium dioxide and the residue washed with absolute ethanol. The solid residue of titanium dioxide was further washed with hot, acetone and then dried up for making it reusable. After the removal of the solvent from the combined filterate under reduced pressure, the organic residue was subjected to column chromatography to obtain pure III. The compound was recrystallized by alcohol-EtOAc mixture.

Characterization of the synthesized compounds

Compound III (a-f):

Compound III (a)

Yield: 78%; m.p:120^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ : 7.25-7.50 (m, 4H, ArH), 7.0 (m, 5H, ArH), 13.0 (s, 1H, -NH), 7.18-7.45 (m, 5H, ArH); ^{13}CNMR (100MHz, $CDCl_3$ / TMS) δ:140.2, 136.7, 136.2, 130.8, 129.9, 129.3, 128.5, 127.0, 125.8, 125.4, 121.6, 120.7, 120.3, 119.6, 111.7, 104.4; EIMS: (m/z): 309.13 (M+). Anal. calcd. For $C_{21}H_{15}N_3$ C: 81.53, H: 4.89, N: 13.58 %

Compound III (b)

Yield: 82%; m.p:75^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ : 7.30-7.49 (m, 4H, ArH), 7.3 (m, 5H, ArH), 13.4 (s, 1H, -NH), 6.52-7.23 (m, 4H, ArH), 4.4 (s, 2H, $-NH_2$); ^{13}CNMR (100MHz, $CDCl_3$ / TMS) δ:146.7, 140.7, 136.5, 136.3, 130.4, 129.1, 127.8, 126.5, 125.3, 125.1, 121.4, 120.5, 120.2, 119.9, 115.6, 111.4, 104.7; EIMS: (m/z): 324.14 (M+). Anal. calcd. For $C_{21}H_{16}N_4$ C: 77.76, H: 4.97, N: 17.27 %

Compound III (c)

Yield: 88%; m.p:89^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ : 7.39-7.52 (m, 4H, ArH), 7.5 (m, 5H, ArH), 13.7 (s, 1H, -NH), 7.22-7.36 (m, 4H, ArH), 2.39 (s, 3H, $-CH_3$); ^{13}CNMR (100MHz, $CDCl_3$ / TMS) δ:140.4, 137.7, 136.9, 136.2, 133.5, 130.7, 129.7, 129.3, 126.9, 125.6, 125.2, 121.2, 120.9, 120.5, 119.4, 111.0, 104.2, 20.5; EIMS: (m/z): 323.14 (M+). Anal. calcd. For $C_{21}H_{17}N_3$ C: 81.71, H: 5.30, N: 12.99 %

Compound III (d)

Yield: 90%; m.p:105^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ : 7.33-7.42 (m, 4H, ArH), 7.9 (m, 5H, ArH), 13.2 (s, 1H, -NH), 6.83-7.37 (m, 4H, ArH), 3.77 (s, 3H, -OCH_3); ^{13}CNMR (100MHz, $CDCl_3$ / TMS) δ:162.0, 140.9, 136.5, 136.6, 130.8, 129.7, 128.8, 128.0, 125.8, 125.3, 121.9, 120.7, 120.7, 120.3, 119.9, 114.6, 111.8, 104.7, 56.6; EIMS: (m/z): 339.14 (M+). Anal. calcd. For $C_{22}H_{17}N_3O$ C: 77.86, H: 5.05, N: 12.38, O: 4.71 %

Compound III (e)

Yield: 80%; m.p:95^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ : 7.28-7.52 (m, 4H, ArH), 7.4 (m, 5H, ArH), 13.9 (s, 1H, -NH), 7.37-7.49 (m, 4H, ArH); ^{13}CNMR (100MHz, $CDCl_3$ / TMS) δ:140.3, 136.9, 136.4, 135.5, 132.3, 130.5, 129.2, 129.0, 125.5, 125.0, 123.1, 121.3, 120.5, 120.3, 119.5, 111.5, 104.4; EIMS: (m/z): 389.04 (M+). Anal. calcd. For $C_{21}H_{14}$ BrN_3 C: 64.96, H: 3.63, Br: 20.58, N: 10.82%

Compound III (f)

Yield: 83%; m.p:115^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ : 7.30-7.49 (m, 4H, ArH), 7.7 (m, 5H, ArH), 13.5 (s, 1H, -NH), 7.33-7.42 (m, 4H, ArH); ^{13}CNMR (100MHz, $CDCl_3$ / TMS) δ:140.5, 136.2, 136.0, 134.6, 133.8, 130.0, 129.6, 129.2, 128.4, 125.3, 125.1, 121.5, 120.6, 120.2, 119.3, 111.3, 104.9; EIMS: (m/z): 343.09 (M+). Anal. calcd. For $C_{21}H_{14}$ ClN_3 C: 73.36, H: 4.10, Cl: 10.31, N: 11.22%

RESULTS AND DISCUSSION

Nitrogen containing heterocycles are ubiquitous systems in nature and are consequently considered as privileged structures in drug discovery. It was reported that various 3-substituted indoles had been used as starting materials for the synthesis of a number of alkaloids, agrochemicals, pharmaceuticals and perfumes. Accordingly the synthesis of indole derivatives has been a major topic in organic and medicinal chemistry over the past several decades.

Several well known bioactive alkaloids are based on indole derivatives. Hence considerable research is underway to develop indole based therapeutic agents. Indole-3-carbinol exhibits antiproliferative activity in many types of human cancer cells [12,13] including estrogen responsive and estrogen-independent breast cancer cell [14,15] and human prostrate cancer cell. [16] Recently it has been reported that indole derivatives such as 3-(2, 5- substituted- 1H- indole-3- yl)-1- phenyl prop-2- en-1- one) exhibited significant antioxidant and DNA cleavage activities. [17] Keeping all these goals here the target compound is synthesized by taking mixture of 1-Phenyl-1H- indole- 2, 3-dione was condensed in an oil-bath with substituted aldehyde , ammonium acetate and titanium dioxide to give the corresponding 2, 8-Diphenyl-1, 3a, 8, 8a-tetrahydro- 1, 3, 8-triaza-cyclopenta[α] indene derivatives respectively according to the scheme given. The structure of these compounds were established on the basis of elemental (C, H, N) and spectral (1H-NMR, 13C-NMR and spectral data) analysis. The ^{1}H- NMR spectrum also revealed one singlet signals at δ 13.0 ppm assignable to the NH of the indole ring.

The synthesized compounds were found to exhibit various biological activities viz. antimicrobial, anticonvulsant, anti-inflammatory and antitubercular etc.

CONCLUSION

The 1, 3, 8-triaza- cyclopenta[α] indene ring is an important pharmacophore in modern drug discovery. This review gives an overview of the various synthetic routes used to form a biologically active 1, 3, 8-triaza- cyclopenta[α] indene moiety as well as the reactions the molecule undergoes to yield various other important molecules. This paper proves to be significant for further research work on the biologically active 1, 3, 8-triaza- cyclopenta[α] indene ring.

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