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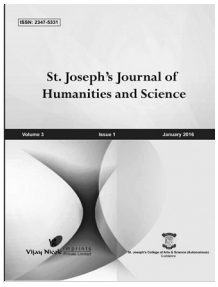

Synthesis of Carbazole Based C-Glycosidic Ketones Catalyzed By L-Proline-Et_3n

G. Anand*

ABSTRACT

Carbazoles alkaloids isolated from natural sources and their synthetic analogues are interesting pharmacophore, reported to posses various biological activity. Most carbazole alkaloids have been isolated from the taxonomically related higher plants of the genus Murraya, Glycosmis, and Clausena from the family Rutaceae. Generally carbazoles are functionalized at the 3- and 6- position due to the highest electron density at these positions. However, recent advances in organic chemistry, such as metal catalysed C-C bond activation and C-C bond formation made the possibility of functionalization at the 2- and 7- position. Carbazole glycosidic ketones were synthesized through the organocatalyzed aldol condensation of 4,6-O-protected-D-glucose-propanone with 9-alkyl-9H- carbazole-3-carbaldehyde. Pyrrolidine and L-proline–triethylamine were used as catalyst, due to decreased reaction time and increased yield, L-proline–triethylamine mixture was found to be better catalyst than pyrrolidine for the Aldol condensation of sugar ketone with alkyl substituted carbazole.

Keywords: Carbazole; Proline; Glycosidic ketone; Ketones

1.0 INTRODUCTION

Carbazoles alkaloids isolated from natural sources and their synthetic analogues are interesting pharmacophore, reported to posses various biological activity. [1] In 1965, Chakraborty et al., isolated murrayanine, A (Figure.1) an antibiotic carbazole alkaloid from Murraya koenigii.[2] Most carbazole alkaloids have been isolated from the taxonomically related higher plants of the genus Murraya, Glycosmis, and Clausena from the family Rutaceae. The genus Murraya represents the richest source of carbazole alkaloids from terrestrial plants. The lower plants from which carbazole alkaloids have been isolated include several different Streptomyces species. [3] Carazostatin a carbazole alkaloid isolated from Streptomyces chromofuscus by Kato et al., was reported for antioxidant activity. Moreover, it was found to be more active than butylated hydroxytoluene (BHT) and α-tocopherol. [4] Carbazole alkaloids and their analogues were also reported to be active against both gram positive and gram negative bacteria.[5] Antitumor, [6] antihypertensive, [7] anticancer, [8] and cardiotonic activity[9] were also reported for the carbazole alkaloids.

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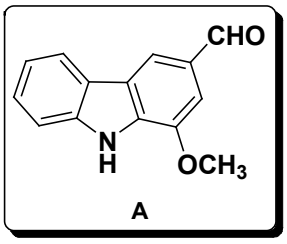


Figure.1: Chemical Structure Murrayanine (A) [2]

A considerable quantity of glycosylated carbazole alkaloids (**Figure. 2**) was also isolated from natural sources. There are two classes of glycosidic carbazole alkaloids, differing both in structure and in mechanism of action. Straurosporine class is characterized by the existence of two bonds between the glycoside and carbazole heterocycle (**B**), these fused structures exhibit potent inhibition of protein kinases.[10] Rebeccamycin (**C**) class of glycosidic carbazole have a single glycosidic linkage and have shown remarkable activity in the poisoning of DNA topoisomerase I.[11] Interest on the isolation and synthesis of carbazole glycosides comes from their potent antineoplastic properties.[12] Generally carbazoles are functionalized at the 3- and 6- position due to the highest electron density at these positions. However, recent advances in organic chemistry, such as metal catalysed C-C bond activation and C-C bond formation made the possibility of functionalization at the 2- and 7- position.[13] Such advances made in the carbazole chemistry lead to development of large number carbazole drug.[14] Carbazole derivatives have also been reported for good application as organic materials. Carbazole and its derivatives are efficient blue emitting and hole-transport materials.[15]

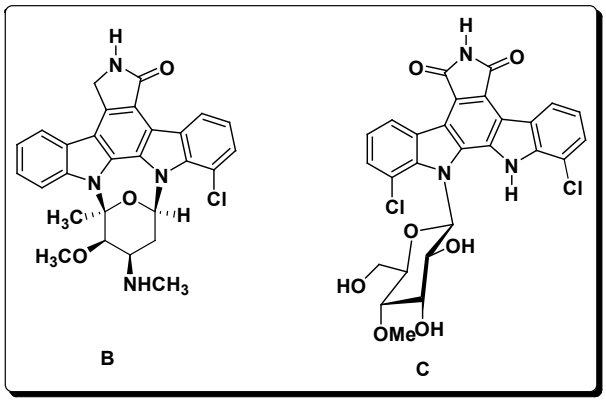


Figure. 2: Chemical Structure of Carbohydrate Based Carbazole Alkaloids Straurosporine (B) and Rebeccamycin (C) [10,11]

Carbazole glycosidic ketones were synthesized by combining 4,6-O-protected-D-glucose-propanone with 9-alkyl-9H- carbazole-3-carbaldehyde catalyzed by L-proline–triethylamine mixture for the Aldol condensation of sugar ketone with alkyl substituted carbazole.

2.0 EXPERIMENTAL

Materials and Methods

Butyraldehyde, paraldehyde, 2,4-pentanedione, pyrrolidene, L-proline, carbazole, bromoethane, bromooctane, bromododecane and bromohexadecane were purchased from Sigma Aldrich chemicals Pvt. Ltd. USA. Con.HCl, Con.H_2SO_4, D-glucose, ethanol, triethyl amine, KOH, $POCl_3$, sodium bicarbonate, were obtained from Sd-fine India. Solvents, such as hexane, chloroform and ethyl acetate were purchased from SRL, India, were of high purity and used without any further purification. Column chromatography was performed on silica gel (100-200 mesh). NMR spectra were recorded on a Bruker DRX 300 MHz instrument in $CDCl_3$ (with few drops of DMSO-d_6). Chemical shifts are referenced to internal TMS.

General Procedure for Pyrrolidine Catalyzed Synthesis of Carbazole Glycosidic Ketone 3(a-h)

1-(4,6-*O*-protected-β-D-Glucopyranosyl)propan-2-one was synthesized from their respective 4,6-*O*-protected-D-glucopyranose derivatives through the $NaHCO_3$ mediated Knoveneagel condensation of 2,4-pentanedione with 4,6-*O*-protected-D-glucopyranose according to literature procedure.[19] 9-Alkyl-3-formyl-carbazole **2**(**a-d**) were prepared by adopting methodology reported by Qiu *et al*.[20]

To a solution of 1 mmol (4,6-*O*-protected-β-D-glucopyranosyl)propan-2-one (**1a**, **1b**) in dry DCM, 10% mol of pyrrolidene (8 µl) and 1 mmol of *N*-alkyl carbazole aldehyde **2**(**a-d**) were added and stirred at room temperature for 48 hrs. After confirming the completion of the reaction through TLC, the DCM in the reaction mixture was evaporated and extracted with EtOAc–water. The ethyl acetate layer was dried over anhyd.Na_2SO_4 and concentrated to dryness. The crude product was further purified by flash column chromatography to obtain pale yellow solid **3(a-h)** with yield of 30-42%.

General procedure for L-proline–triethylamine catalyzed synthesis of carbazole glycosidic ketone 3(a-h)

To a solution of 1 mmol (4,6-*O*-protected-β-D-glucopyranosyl)propan-2-one (**1a**, **1b**), in dry ethanol, 10% mol of L-proline (0.012 g), 15% mol of triethylamine (20 µl) and 1 mmol of *N*-alkyl-monoformyl carbazole **2(a-d)** were added and stirred at room temperature for 30 hrs. After confirming the completion of the reaction through TLC. Ethanol in the reaction mixture was evaporated under reduced pressure and extracted with EtOAc–water. The ethyl acetate layer was dried over anhyd.Na_2SO_4 and concentrated to dryness. The crude product was further purified by flash column chromatography to obtain pale yellow solid **3(a-h)** with yield 69-92 %.

***(E)*-1-(4,6-*O*-ethylidene-β-D-glucopyranosyl)-4-(9-ethyl-9*H*-carbazole)but-3-en-2-one (3a)**

Compound **3a** was obtained by the aldol condensation of ethylidene-β-*C*-glycosidic-ketone, **1a** (1 mmol, 0.246 g) with 9-ethyl-9*H*-carbazole-3-carbaldehyde, **2a** (1 mmol, 0.223 g) as a pale yellow solid.

Mp 189-192 °C; **^{1}H NMR** (300 MHz, $CDCl_3$): δ_H 8.35(s, 1H, Ar-*H*), 8.14(d, *J* = 7.8 Hz, 1H, Ar-*H*), 7.77(d, *J* = 15.9 Hz, 1H, *H*C=CH), 7.75(m, 7.75-7.73, 1H, Ar-*H*), 7.52(m, 7.52-7.49, 3H, Ar-*H*), 7.28(m, 7.28-7.25, 1H, Ar-*H*), 6.86(d, *J* = 15.9 Hz, 1H, HC=C*H*), 5.29(d, *J* = 5.4 Hz, 1H, Sacc-O*H*), 5.21(d, *J* = 5.4 Hz, 1H, Sacc-O*H*), 4.70(d, *J* = 5.1 Hz,1H, Ace-*H*), 4.44(m, 4.44-4.40, 2H, N-CH_2), 4.04(m, 4.04-3.99, 1H, Sacc-*H*), 3.80(t, *J* = 9 Hz, 1H, Ano-*H*), 3.56(m, 3.56-3.53, 2H, Sacc-*H*), 3.28(m, 3.28-3.22 3H, Sacc-*H* & CH_2CO), 3.17(m, 3.17-3.16, 1H, Sacc-*H*), 2.90(m, 2.90-2.87, 1H, Sacc-*H*), 1.43(t, *J* = 6.9 Hz, 3H, CH_3), 1.30(t, *J* = 4.8 Hz, 3H, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$): δ_C 196.9(1C, *C*=O), 143.5(1C, Ar-*C*), 140.4(1C, H*C*=CH), 139.5(1C, Ar-*C*), 125.6(1C, Ar-*C*), 125.3(1C, Ar-*C*), 124.5(1C, Ar-*C*), 122.9(1C, Ar-*C*), 122.3(1C, HC=*C*H), 121.7(1C, Ar-*C*), 120.6(1C, Ar-*C*), 119.7(1C, Ar-*C*), 118.8(1C, Ar-*C*), 108.4(1C, Ar-*C*), 108.3(1C, Ar-*C*), 98.3(1C, Ace-*C*), 79.9(1C, Ano-*C*), 76.2(1C, Sacc-*C*), 73.8(2C, Sacc-*C*), 69.6(1C, Sacc-*C*), 67.3(1C, Sacc-*C*), 42.4(1C, N-*C*H_2), 36.8(1C, O*C*H_2), 19.6(1C, *C*H_3), 13.0(1C, *C*H_3).

***(E)*-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-(9-ethyl-9*H*-carbazole)but-3-en-2-one (3b)**

Compound **3b** was obtained by the aldol condensation of butylidene-β-*C*-glycosidic-ketone, **1b** (1 mmol, 0.274 g) with 9-ethyl-9*H*-carbazole-3-carbaldehyde, **2a** (1 mmol, 0.223 g) as a pale yellow solid.

Mp180-184 °C; **^{1}H NMR** (300 MHz, $CDCl_3$): δ_H 8.22(s, 1H, Ar-*H*), 8.04(d, *J* = 7.5 Hz, 1H, Ar-*H*), 7.76(d, *J* = 15.9 Hz, 1H, *H*C=CH), 7.63(d, *J* = 8.4 Hz, 1H, Ar-*H*), 7.47(m, 7.47-7.42, 1H, Ar-*H*), 7.38(m, 7.38-7.30, 2H, Ar-*H*), 7.23(d, *J* = 7.5 Hz, 1H, Ar-*H*), 6.77(d, *J* = 15.9 Hz, 1H, HC=C*H*), 4.48(m, 4.48-4.44, 1H, Ace-*H*), 4.35(m, 4.35-4.27, 2H, N-CH_2), 4.11(m, 4.11-4.03, 1H, Sacc-*H*), 3.80(m, 3.80-3.73, 1H, Sacc-*H*), 3.61(t, *J* = 9 Hz, 1H, Ano-*H*), 3.42(m, 3.42-3.24, 4H, Sacc-*H* & CH_2CO), 3.17(m, 3.17-3.06, 2H, Sacc-*H* & O*H*), 2.89(m, 2.89-2.80, 1H, Sacc-*H*), 2.62(m, 2.62-2.54, 1H, Sacc-*H*), 1.60(m, 1.60-1.54, 2H, CH_2), 1.41(m, 1.41-1.34, 2H, CH_2), 0.87(m, 0.87-0.82, 6H, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$): δ_C 196.8(1C, *C*=O), 145.7(1C, Ar-*C*), 141.6(1C, H*C*=CH), 140.5(1C, Ar-*C*), 126.4(1C, Ar-*C*), 126.2(2C, Ar-*C*), 123.5(1C, Ar-*C*), 123.4(1C, Ar-*C*), 122.8(1C, Ar-*C*), 121.8(1C, HC=*C*H), 120.6(1C, Ar-*C*), 119.8(1C, Ar-*C*), 108.9(2C, Ar-*C*), 102.5(1C, Ace-*C*), 80.4(1C, Ano-*C*), 75.8(1C, Sacc-*C*), 74.8(1C, Sacc-*C*), 74.3(1C, Sacc-*C*), 70.6(1C, Sacc-*C*), 68.4(1C, Sacc-*C*), 46.2(1C, N-*C*H_2), 37.8(1C, O*C*H_2), 36.2(1C, *C*H_2), 30.9(1C, *C*H_2), 17.5(1C, *C*H_3), 13.9(1C, *C*H_3).

***(E)*-1-(4,6-*O*-ethylidene-β-D-glucopyranosyl)-4-(9-octyl-9*H*-carbazole)but-3-en-2-one (3c)**

Compound **3c** was obtained by the aldol condensation of ethylidene-β-*C*-glycosidic-ketone, **1a** (1 mmol, 0.246 g) with 9-octyl-9*H*-carbazole-3-carbaldehyde, **2b** (1 mmol, 0.307 g) as a pale yellow solid.

Mp 178-180 °C; **^{1}H NMR** (300 MHz, $CDCl_3$): δ_H 8.19(s, 1H, Ar-*H*), 8.02(d, *J* = 7.5 Hz, 1H, Ar-*H*), 7.75(d, *J* = 15.9 Hz, 1H, *H*C=CH), 7.58(d, *J* = 6 Hz, 1H, Ar-*H*), 7.42(m, 7.42-7.40, 1H, Ar-*H*), 7.33(d, *J* = 8.1 Hz, 1H, Ar-*H*), 7.29(d, *J* = 8.7 Hz, 1H, Ar-*H*), 7.27(m, 7.27-7.19, 1H, Ar-*H*), 6.76(d, *J* = 15.9 Hz, 1H, HC=C*H*), 4.64(m, 4.64-4.62, 1H, Ace-*H*), 4.19(t, *J* = 6.6 Hz, 2H, N-CH_2), 4.09(m, 4.09-4.04, 1H, Sacc-*H*), 3.90(m, 3.90-3.87, 1H, Sacc-*H*), 3.69(t, *J* = 8.7 Hz, 1H, Ano-*H*), 3.42(m, 3.42-3.20, 6H, Sacc-*H,* O*H* & CH_2CO), 3.12(m, 3.12-3.06, 1H, Sacc-*H*), 2.99(m,

2.99-2.94, 1H, Sacc-*H*), 1.80(m, 1.80-1.75, 2H, CH_2), 1.33(m, 1.33-1.29, 6H, CH_2), 1.25(m, 1.25-1.16, 7H, CH_2 & CH_3), 0.78(t, *J* = 6.3 Hz, 3H, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$): δ_C 197.4(1C, *C*=O), 144.7(1C, Ar-*C*), 141.0(1C, H*C*=CH), 139.9(1C, Ar-*C*), 125.3(1C, Ar-*C*), 125.1(1C, Ar-*C*), 124.1(1C, Ar-*C*), 122.4(1C, Ar-*C*), 122.3(1C, Ar-*C*), 121.7(1C, HC=*CH*), 120.8(1C, Ar-*C*), 119.5(1C, Ar-*C*), 118.7(1C, Ar-*C*), 108.1(2C, Ar-*C*), 98.6(1C, Ace-*C*), 79.4(1C, Ano-*C*), 75.5(1C, Sacc-*C*), 74.2(1C, Sacc-*C*), 73.8(1C, Sacc-*C*), 69.5(1C, Sacc-*C*), 67.3(1C, Sacc-*C*), 42.4(1C, N-CH_2), 42.3(1C, CH_2CO), 30.7(1C, *C*H_2), 28.3(1C, *C*H_2), 28.1(1C, *C*H_2), 27.9(1C, *C*H_2), 26.2(1C, *C*H_2), 21.6(1C, *C*H_2), 19.3(1C, *C*H_3), 13.0(1C, *C*H_3).

(*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-(9-octyl-9*H*-carbazole)but-3-en-2-one (3d):

Compound **3d** was obtained by the aldol condensation of butylidene-β-*C*-glycosidic-ketone, **1b** (1 mmol, 0.274 g) with 9-octyl-9*H*-carbazole-3-carbaldehyde, **2b** (1 mmol, 0.307 g) as a pale yellow solid.

Mp 163-165 °C; **^{1}H NMR** (300 MHz, $CDCl_3$): δ_H 8.28(s, 1H, Ar-*H*), 8.10(d, *J* = 7.8 Hz, 1H, Ar-*H*), 7.83(d, *J* = 15.9 Hz, 1H, *H*C=C), 7.69(d, *J* = 9 Hz, 1H, Ar-*H*), 7.50(m, 7.50-7.48, 1H, Ar-*H*), 7.43(m,7.43-7.38, 2H, Ar-*H*), 7.27(d, *J* = 8.7Hz, 1H, Ar-*H*), 6.84(d, *J* = 16.2 Hz, 1H, C=C*H*), 4.54(t, *J* = 5.1 Hz, 1H, Ace-*H*), 4.29(t, *J* = 6.9 Hz, 2H, N-CH_2), 4.00(m, 4.00-3.93, 1H, Sacc-*H*), 3.75(t, *J* = 9 Hz, 1H, Ano-*H*), 3.49(m, 3.49-3.42, 3H, Sacc-O*H,* CH_2CO), 3.40(m, 3.40-3.34, 2H, Sacc-*H*), 3.32(m, 3.32-3.30, 2H, Sacc-*H*), 3.27(m, 3.27-3.24, 1H, Sacc-*H*), 3.07(m, 3.07-3.02, 1H, Sacc-*H*), 1.90(m, 1.90-1.84, 2H, CH_2), 1.65(m, 1.65-1.60, 6H, CH_2), 1.44(m, 1.44-1.24, 8H, CH_2), 0.94(m, 0.94-0.84, 6H, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$): δ_C 198.3(1C, *C*=O), 145.7(1C, Ar-*C*), 142.1(1C, *C*=C), 140.9(1C, Ar-*C*), 126.4(1C, Ar-*C*), 126.1(1C, Ar-*C*), 125.2(1C, Ar-*C*), 123.4(1C, Ar-*C*), 122.7(1C, Ar-*C*), 121.8(1C, C=*C*), 120.5(1C, Ar-*C*), 119.7(1C, Ar-*C*), 109.2(2C, Ar-*C*), 102.5(1C, Ace-*C*), 80.5(1C, Ano-*C*), 76.4(1C, Sacc-*C*), 75.4(1C, Sacc-*C*), 74.8(1C, Sacc-*C*), 70.6(1C, Sacc-*C*), 68.4(1C, Sacc-*C*), 43.5(1C, N-CH_2), 43.3(1C, CH_2CO), 36.3(1C, *C*H_2), 30.8(1C, *C*H_2), 29.3(1C, *C*H_2), 29.1(1C, *C*H_2), 28.9(1C, *C*H_2), 27.3(1C, *C*H_2), 22.6(1C, *C*H_2), 17.5(1C, *C*H_2), 14.1(1C, *C*H_3), 13.9(1C, *C*H_3).

(*E*)-1-(4,6-*O*-ethylidene-β-D-glucopyranosyl)-4-(9-dodecyl-9*H*-carbazole)but-3-en-2-one (3e)

Compound 3e was obtained by the aldol condensation of ethylidene-β-C-glycosidic-ketone, 1a (1 mmol, 0.246 g) with 9-dodecyl-9H-carbazole-3-carbaldehyde, 2c (1 mmol, 0.363 g) as a pale yellow solid.

Mp 175-178 °C; 1H NMR (300 MHz, CDCl3): δH 8.21(s, 1H, Ar-H), 8.02(d, J = 7.8 Hz, 1H, Ar-H), 7.75(d, J = 15.9 Hz, 1H, HC=CH), 7.60(d, J = 7.5 Hz, 1H, Ar-H), 7.43(t, J = 7.5 Hz, 1H, Ar-H), 7.32(t, J = 9.6 Hz, 2H, Ar-H), 7.23(m,7.23-7.19 1H, Ar-H), 6.76(d, J = 15.9 Hz, 1H, HC=CH), 4.66(m, 4.66-4.64 1H, Ace-H), 4.21(d, J= 6.9Hz, 2H, N-CH2), 4.10(m, 4.10-4.05, 1H, Sacc-H), 3.90(m, 3.90-3.72, 1H, Sacc-H), 3.69(t, J = 8.7 Hz, 1H, Ano-H), 3.43(m, 3H, 3.43-3.34, Sacc-H), 3.33(m, 2H, 3.33-3.22 Sacc-H), 3.07(m, 3.07-3.06, 1H, Sacc-H,) 3.00(m, 3.00-2.93, 2H, Sacc-H), 1.79(t , J = 6.6 Hz, 2H, CH2), 1.60(m, 1.60-1.28 8H, CH2), 1.26(m, 1.26-1.22, 13H, CH2 & CH3), 0.82(m, 0.82-0.78, 3H, CH3); 13C NMR (75 MHz, CDCl3): δC 197.3(1C, C=O), 144.7(1C, Ar-C), 141.0(1C, HC=CH), 139.9(1C, Ar-C), 125.3(1C, Ar-C), 125.1(1C, Ar-C), 124.1(1C, Ar-C), 122.3(1C, HC=CH), 121.7(2C, Ar-C), 120.7(1C, Ar-C), 119.5(1C, Ar-C), 118.7(1C, Ar-C), 108.1(2C, Ar-C), 98.6(1C, Ace-C), 79.4(1C, Ano-C), 75.3(1C, Sacc-C), 74.3(1C, Sacc-C), 73.9(1C, Sacc-C), 69.5(1C, Sacc-C), 67.3(1C, Sacc-C), 42.5(1C, N-CH2), 42.3(1C, OCH2), 30.9(1C, CH2), 28.6(1C, CH2), 28.4(1C, CH2), 28.3(1C, CH2), 28.2(2C, CH2), 27.9(1C, CH2), 26.2(1C, CH2), 21.6(1C, CH2), 19.3(1C, CH3), 13.0(1C, CH3).

(E)-1-(4,6-O-butylidene-β-D-glucopyranosyl)-4-(9-dodecyl-9H-carbazole) but-3-en-2-one (3f)

Compound 3f was obtained by the aldol condensation of butylidene-β-C-glycosidic-ketone, **1b** (1 mmol, 0.274 g) with 9- dodecyl-9H-carbazole-3-carbaldehyde, 2c (1 mmol, 0.363 g) as a pale yellow solid.

Mp 163-165oC; 1H NMR (300 MHz, CDCl3): δH 8.27(s, 1H, Ar-H), 8.08(d, J = 7.8 Hz, 1H, Ar-H), 7.81(d, J = 15.9 Hz, 1H, HC=CH), 7.66(d, J = 8.4 Hz, 1H, Ar-H), 7.50(m, 7.50-7.47, 1H, Ar-H), 7.42(m, 7.42-7.36, 2H, Ar-H), 7.30(m, 7.30-7.23, 2H, Ar-H), 6.83(d, J = 15.9 Hz, 1H, HC=CH), 4.54(m, 4.54-4.52, 1H, Ace-H), 4.27(t, J = 7.2 Hz, 2H, N-CH2), 4.17(m, 4.17-4.10, 1H, Sacc-H), 3.96(m, 3.96-3.75, 1H, Sacc-H), 3.75(t, J = 8.7 Hz, 1H, Ano-H), 3.49(m, 3.49-3.39, 4H, Sacc-H), 3.37(m, 3.37-3.27, 2H, Sacc-H),

3.24(m, 3.24-3.13, 2H, Sacc-H), 3.06(m, 3.06-2.99, 2H, Sacc-H), 1.84(d, J = 6.9 Hz, 2H, CH2), 1.65(m, 1.65-1.60, 4H, CH2), 1.44(m, 1.44-1.38, 2H, CH2), 1.32(m, 1.32-1.29, 16H, CH2), 0.94(m, 0.94-0.85, 6H, CH3); 13C NMR (75 MHz, CDCl3): δC 198.3(1C, C=O), 145.7(1C, Ar-C), 142.0(1C, Ar-C), 140.9(1C, HC=CH), 126.3(1C, Ar-C), 126.1(1C, Ar-C), 125.1(1C, Ar-C), 123.4(1C, Ar-C), 123.3(1C, Ar-C), 122.7(1C, Ar-C), 121.8(1C, HC=CH), 120.5(1C, Ar-C), 119.7(1C, Ar-C), 109.2(2C, Ar-C), 102.5(1C, Ace-C), 80.5(1C, Ano-C), 76.4(1C, Sacc-C), 75.4(1C, Sacc-C), 74.8(1C, Sacc-C), 70.6(1C, Sacc-C), 68.4(1C, Sacc-C), 43.5(1C, N-CH2), 43.3(1C, CH2CO), 36.3(1C, CH2), 32.0(2C, CH2), 29.6(2C, CH2), 29.5(1C, CH2), 29.4(1C, CH2), 29.3(1C, CH2) , 29.3(1C, CH2), 28.9(1C, CH2), 27.3(1C, CH2), 22.7(1C, CH2), 17.5(2C, CH3).

(*E*)-1-(4,6-*O*-ethylidene-β-D-glucopyranosyl)-4-(9-hexadecyl-9*H*-carbazole)but-3-en-2-one (3g)

Compound 3g was obtained by the aldol condensation of ethylidene-β-C-glycosidic-ketone, **1a** (1 mmol, 0.246g) with 9-hexadecyl-9H-carbazole-3-carbaldehyde, 2d (1 mmol, 0.419 g) as a pale yellow solid.

Mp 172-175 °C; 1H NMR (300 MHz, CDCl3): δH 8.21(s, 1H, Ar-H), 8.03(d, J = 7.5 Hz, 1H, Ar-H), 7.76(d, J = 15.9 Hz, 1H, HC=CH), 7.62(d, J = 7.5 Hz, 1H, Ar-H), 7.43(m, 7.43-7.41, 1H, Ar-H), 7.36 (m, 7.36-7.31, 2H, Ar-H), 7.22(d, J = 7.2 Hz, 1H, Ar-H), 6.77(d, J = 15.9 Hz, 1H, C=CH), 4.66(m, 4.66-4.64, 1H, Ace-H), 4.22(t, J= 7.2 Hz, 2H, N-CH2), 4.20(m, 4.20-4.05, 1H, Sacc-H), 3.89(m, 3.89-3.87, 1H, Sacc-H), 3.68(t, J = 8.7 Hz, 1H, Ano-H), 3.43(m, 3.43-3.39, 2H, CH2CO), 3.37(m, 3.37-3.33, 2H, Sacc-H & OH), 3.31(m, 3.31-3.20, 2H, Sacc-H & OH), 3.07(m, 3.07-2.93, 2H, Sacc-H,), 1.82(m, 1.82-1.77, 2H, CH2), 1.31(m, 1.31-1.20, 8H, CH2), 1.18(m, 1.18-1.16, 21H, CH2 & CH3), 0.81(t, J = 6.9 Hz, 3H, CH3); 13C NMR (75 MHz, CDCl3): δC 195.8(1C, C=O), 144.1(1C, Ar-C), 142.1(1C, HC=C), 139.7(1C, Ar-C), 125.8(1C, Ar-C), 125.6(2C, Ar-C), 124.8(1C, Ar-C), 122.3(1C, C=C), 122.2(1C, Ar-C), 121.3(1C, C=CH), 119.5(1C, Ar-C), 118.4(1C, Ar-C), 108.1(1C, Ar-C), 107.9(1C, Ar-C), 99.3(1C, Ace-C), 80.1(1C, Ano-C), 76.1(1C, Sacc-C), 74.3(1C, Sacc-C), 73.9(1C, Sacc-C), 68.1(1C, Sacc-C), 66.3(1C, Sacc-C), 43.5(1C, N-CH2), 43.0(1C, OCH2), 30.7(1C, CH2), 28.6(1C, CH2), 28.4(2C, CH2), 28.2(2C, CH2), 28.0(2C, CH2), 27.3(2C, CH2), 26.5(2C, CH2), 21.8(2C, CH2), 18.5(1C, CH3), 13.4(1C, CH3).

(*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-(9-hexadecyl-9*H*-carbazole)but-3-en-2-one (3h)

Compound **3h** was obtained by the Aldol condensation of butylidene-β-*C*-glycosidic-ketone, **1b** (1 mmol, 0.274 g) with 9-hexadecyl-9*H*-carbazole-3-carbaldehyde, **2d** (1 mmol, 0.419 g) as a pale yellow solid.

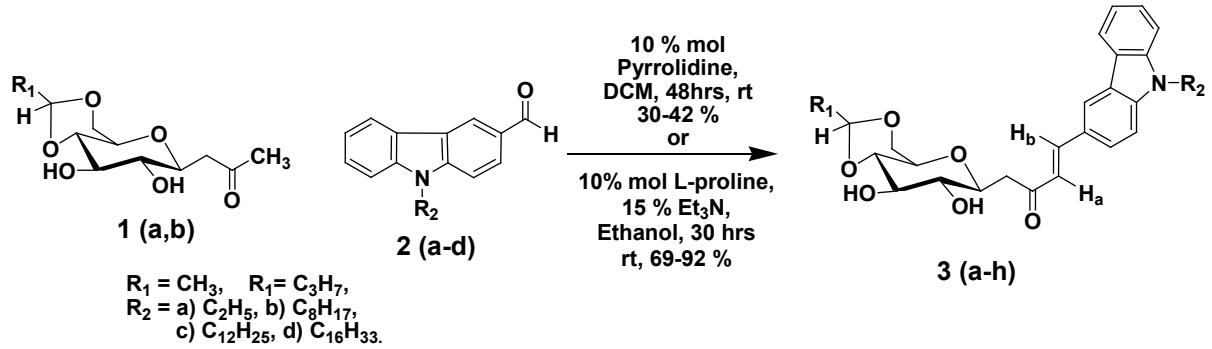
Mp 150-152 °C; 1H NMR (300 MHz, CDCl3): δH 8.22(s, 1H, Ar-H), 8.04(d, J = 7.8 Hz, 1H, Ar-H), 7.76(d, J = 15.9 Hz, 1H, HC=CH), 7.62(d, J = 7.5 Hz, 1H, Ar-H), 7.46(m, 7.46-7.41, 1H, Ar-H), 7.37(m, 7.37-7.31, 2H, Ar-H), 7.23(d, J = 7.2 Hz, 1H, Ar-H), 6.77(d, J = 15.9 Hz, 1H, HC=CH), 4.66(m, 4.66-4.64, 1H, Ace-H), 4.23(t, J= 6.0 Hz, 2H, N-CH2), 4.10(m, 4.10-4.05, 1H, Sacc-H), 3.90(m, 3.90-3.87, 1H, Sacc-H), 3.68(t, J = 8.7 Hz, 1H, Ano-H), 3.43(m, 3.43-3.39, 2H, CH2CO), 3.37(m, 3.37-3.33, 2H, Sacc-H & OH), 3.27(m, 3.27-3.19, 2H, Sacc-H & OH), 3.07(m, 3.07-2.99, 2H, Sacc-H,), 1.80(m, 1.82-1.78, 2H, CH2), 1.58(m, 1.58-1.54, 2H, CH2), 1.31(m, 1.31-1.28, 10H, CH2), 1.27(m, 1.27-1.16, 18H, CH2), 0.81(t, J = 6.9 Hz, 6H, CH3); 13C NMR (75 MHz, CDCl3): δC 196.3(1C, C=O), 143.2(1C, Ar-C), 140.0(1C, HC=C), 138.9(1C, Ar-C), 127.3(1C, Ar-C), 125.4(2C, Ar-C), 123.1(1C, Ar-C), 122.8(1C, Ar-C), 122.4(1C, Ar-C), 121.6(1C, C=CH), 119.3(1C, Ar-C), 118.3(1C, Ar-C), 108.1(2C, Ar-C), 101.5(1C, Ace-C), 80.8(1C, Ano-C), 76.5(1C, Sacc-C), 74.5(1C, Sacc-C), 74.2(1C, Sacc-C), 68.9(1C, Sacc-C), 66.9(1C, Sacc-C), 43.1(1C, N-CH2), 42.8(1C, OCH2), 35.8(1C, CH2), 30.9(1C, CH2), 29.1(1C, CH2), 28.7(2C, CH2), 28.5(3C, CH2), 28.1(2C, CH2), 27.0(1C, CH2), 26.8(1C, CH2), 26.5(2C, CH2), 21.3(2C, CH2), 13.5(1C, CH3), 13.1(1C, CH3).

3.0 RESULTS AND DISCUSSION

1-(4,6-O-Ethylidene-β-D-glucopyranosyl)propan-2-one (1a) and 1-(4,6-O-butylidene-β-D-glucopyranosyl) propan-2-one (1b) were prepared according to the literature.[19] 9-Alkyl-9H-3-formyl carbazole 2 (a-d) were synthesized by vilsmeier formylation as reported by Qiu et. al.[20] By this method a quantitative amount of monoformylated product was obtained and the product formation has been confirmed by 1H and 13C NMR spectral analysis. Aldol condensation of sugar ketone 1(a-b) with carbazole aldehyde 2 (a-d) lead to the formation of (E)-(4,6-O-protected-β-D-glucopyranosyl)-4-(9-alkyl-9-carbazole)but-3-en-2-one 3(a-h). Two types of organocatalysts were used for

the aldol condensation of sugar ketone and carbazole aldehyde (Scheme. 1) they are pyrrolidene as reported by Bisht et al.,[21] and L-proline with triethlyamine reported by Wang et al.[22] It was observed that L-proline–triethyl amine was found to be better catalyst for the condensation of sugar with alkyl substituted carbazole aldehyde when compared to pyrrolidine. L-Proline–triethylamine catalyst resulted in 69-92 % of product formation, while 30-42 % of yield was obtained for pyrrolidine catalyst (Table. 1). Decrease in the yield was observed with increase in the alkyl chain length on carbazole. This may be due to increases in the electron density on the carbazole ring which subsequently decreases the electrophilicity of carbonyl carbon.[23] Formation of the carbazole glycosidic ketone 3(a-h) was confirmed by the 1H and 13C NMR. The 1H NMR spectra of carbazole glycosidic ketone 3(a-h) shows peak around 0.81-1.84 ppm corresponds to alkyl chain. The sugar protons appeared at the range of 2.94-4.66 ppm. The anomeric proton of the D-glucose unit was found as triplet around 3.61-3.80 ppm with the coupling constant of 8.7-9.0 Hz. Based on higher coupling constant of the anomeric proton, it is confirmed that the D-glucose in the carbazole glycosidic ketones 3(a-h) exist as β anomer. From the peaks appeared at region of 6.76-8.21 ppm, the presence of the aromatic unit was identified. The doublet around 6.76-6.86 and 7.75-7.81 ppm corresponds to Ha and Hb protons with coupling constant of 15.9-16.2 Hz,

Table.1 Synthesis of Carbazole Glycosidic Ketone 3(a-h)



Compound	R1	R2	Catalysts	
			Pyrrolidene (Yield %)	L-proline-Et3N (Yield %)
3a	CH3 (1a)	C2H5 (2a)	42	92
3b	C3H7 (1b)	C2H5 (2a)	40	89
3c	CH3 (1a)	C8H17 (2b)	37	85
3d	C3H7 (1b)	C8H17 (2b)	36	83
3e	CH3 (1a)	C12H25 (2c)	36	77
3f	C3H7 (1b)	C12H25 (2c)	35	72
3g	CH3 (1a)	C16H33 (2d)	31	72
3h	C3H7 (1b)	C16H33 (2d)	30	69

which shows that the α, β-unsaturated glycosidic ketones 3(a-h) exist as "trans" isomer. In 13C NMR spectrum of the carbazole glycosidic ketone 3(a-h), the presence of the alkyl chain is confirmed from the peak in the region 13-44 ppm and peaks which appeared in the region of 67-98 ppm are due to saccharide skeleton. The acetal carbon of the ethylidene derivatives (3a, 3c, 3eand 3g) appeared around 98 ppm, whereas for the butylidene derivatives (3b, 3d, 3f and 3h) it was found around 102 ppm. Aromatic and alkenic carbons appear in the region of 108-146 ppm. The peaks appeared around 196-198 ppm corresponds to carbonyl carbon in the glycosidic ketone.

4.0 CONCLUSION

Carbazole glycosidic ketones were synthesized through the organocatalyzed aldol condensation of 4,6-*O*-protected-D-glucose-propanone with 9-alkyl -9*H*- carbazole-3-carbaldehyde. Pyrrolidine and L-proline–triethylamine were used as catalyst, due to decreased reaction time and increased yield, L-proline–triethylamine mixture was found to be better catalyst than pyrrolidine for the Aldol condensation of sugar ketone with alkyl substituted carbazole. The synthesized carbazole glycosides were characterized using ^{1}H and ^{13}C NMR.

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