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Note

Syntheses of novel derivatives of 2-acetylfuro[2,3-*a*]carbazoles, benzo[1,2-*b*]-1,4-thiazepino[2,3-*a*]carbazoles and 1-acetyloxycarbazole-2-carbaldehydes

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An elegant one pot syntheses of the titled compounds **3a-d**, **4a-d** and **6a-d** have been presented starting from 1-hydroxycarbazole-2-carbaldehydes **2a-d** in good yields. Treatment of 1-hydroxycarbazole-2-carbaldehydes **2a-d** with chloroacetone and with *o*-aminothiophenol have afforded the novel 2-acetylfuro[2,3-*a*]carbazoles **3a-d** and benzo-[1,2-*b*]-1,4-thiazepino[2,3-*a*]carbazoles **4a-d** respectively. Further carbazoles **2a-d** are treated with phenyl acetic acid in an attempt to synthesize 3-phenyl-2-oxopyrano[2,3-*a*]-carbazoles **5a-d**, but the reaction did not proceed in the anticipated direction and only acetyl derivatives **6a-d** are obtained. All the products thus obtained from these reactions are well characterized by spectroscopic and analytical data.

Keywords: 1-hydroxycarbazole-2-carbaldehydes, *o*-aminothiophenol, 2-acetylfuro carbazoles, benzo carbazoles, phenyl oxopyranocarbazoles

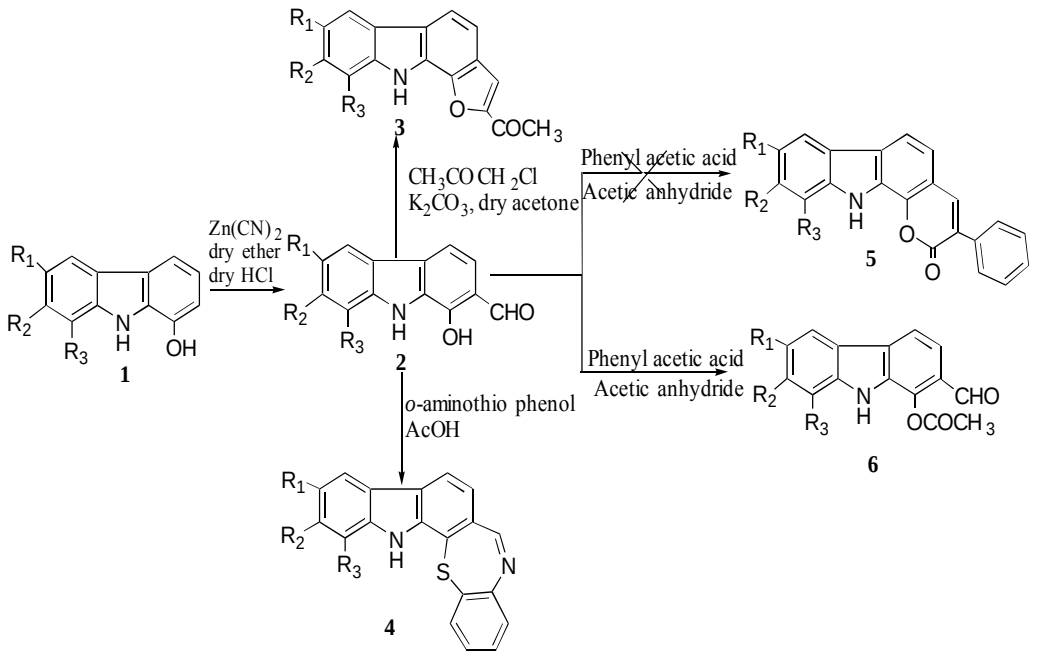
IPC Code: Int.Cl.[8] C07D

The synthesis of substituted carbazoles[1] has attracted considerable attention in recent years as class of these compounds constitute structural frameworks of several naturally occurring compounds, displaying a wide range of biological activity. The therapeutic importance of carbazole derivatives are well established[2-9]. Many elegant approaches have been developed for the synthesis of heterocyclo-fused carbazoles[10] related natural products involving[*b*]-annulations of indoles. Benzodihydro[*a*]carbazoles have been reported as starting compounds for the synthesis of various drugs and possess important biological, pharmacological and medicinal activities[11]. Pyridocarbazoles of both natural and synthetic origin are having significant importance because of their remarkable multimodality of biological action[12]. Based on the above facts, it was aimed to synthesize furo[2,3-*a*]carbazoles, benzo[1, 2-*b*]-1,4-thiazepino[2, 3-*a*]carbazoles and pyrano[2, 3-*a*]carbazoles starting from 1-hydroxycarbazole-2-carbaldehydes[13] under different reaction conditions using simple methodologies.

The required precursor 1-hydroxycarbazole-2-carbaldehydes **2** were prepared from 1-hydroxy-carbazoles according to our reported procedure[9,13]. Reaction of **2a** with chloroacetone in presence of potassium carbonate in dry acetone afforded the product 2-acetyl-7-methylfuro[2,3-*a*]carbazole **3a** in 80% yield. The structure of the **3a** was confirmed from its spectral and analytical studies as discussed. The ^{1}H NMR spectrum **3a** displayed two singlets at δ 2.49 and at 2.61 due to C_7-CH_3 and C_2-$COCH_3$ protons respectively. Three one proton doublets centered at δ 7.27 (J = 8.08 Hz), 7.46 (J = 8.08 Hz) and 7.51 (J = 8.24 Hz) corresponding to C_8-H, C_9-H, and C_4-H protons respectively. A singlet appeared at δ 7.97 was due to C_6-H and a multiplet resonated at 8.06-8.08 corresponding to two protons was due to C_5-H and C_3-H. In addition to this broad singlet at δ 12.11 was ascribable to carbazole-NH. This was supported by the electron impact mass spectrum of the compound which displayed the molecular ion peak at m/z 263, and also elemental analysis also agreed well with the molecular formula $C_{17}H_{13}NO_2$. (**Scheme I, Tables I** and **II**).

The product 10-methylbenzo[1,2-*b*]-1,4-thiazepino[2,3-*a*]carbazole **4a** was obtained by the treatment of **2a** with *o*-aminothiophenol in gl. acetic acid, and well characterized using its spectral and analytical data. Its IR spectrum revealed the presence of –C=N group by exhibiting a strong absorption at 1635 cm^{-1}. The ^{1}H NMR spectrum of **4a** in $CDCl_3$ showed a singlet at δ 2.54 assignable for C_{10}-CH_3. The complex multiplet at δ 7.25-7.98 is assigned for nine aromatic protons. The signals corresponding to carbazole-NH and C_5-H were observed at δ 8.78 and 13.00 as a broad singlet and a singlet respectively. This was also supported by the mass spectrum of the compound which displayed the molecular ion peak at m/z 314. The CHN analysis of the compound **4a** was in good agreement with the proposed molecular formula $C_{20}H_{14}N_2S$, which also gave considerable support to the structure of **4a** (**Scheme I, Tables I** and **II**).

Further, the reaction of **2a** with phenyl acetic acid in acetic anhydride at 120°C was carried out with an



1-6 **a** : $R_1 = CH_3$, $R_2 = R_3 = H$
b : $R_1 = R_3 = H$, $R_2 = CH_3$
c : $R_1 = R_2 = H$, $R_3 = CH_3$
d : $R_1 = R_2 = R_3 = H$

Scheme I

interest that the reaction would proceed as shown in **Scheme I**. At the end, this attempt yielded a single product, with m.p. 175°C. The IR spectrum of this compound showed strong absorptions at 3247, 1759, and 1666 cm^{-1} which are accountable for -NH, ester carbonyl and aldehyde stretchings respectively. The ^1H NMR spectrum exhibited following resonance, two singlets, each for three protons at δ 2.50 and 2.51, a multiplet at 7.31-8.01 for five protons and two singlets, each for one proton at 8.16 and 10.19 respectively. Two singlets, each for three protons at δ 2.50 and 2.51 for C_6-CH_3 and C_1-$OCOCH_3$ protons respectively. The aromatic cluster appeared at δ 7.31-8.01 with five proton integration was due to C_3, C_4, C_5, C_7 and C_8 protons accordingly. The signals due to indole -NH and C_2-CHO resonated as a broad singlet and a singlet at δ 8.16 and 10.19 respectively. The non-existence of signals in the olefinic region revealed that the product formed was not the expected one. This was also supported by the electron impact mass spectrum of the compound which displayed the molecular ion peak at *m/z* 267, whereas the expected product requires the molecular ion at *m/z* 325. The elemental analysis was also in good agreement with the molecular formula $C_{16}H_{13}NO_3$. Hence, both spectral and analytical data indicated that the reaction did not afford the expected 3-phenyl-2-oxopyrano[2, 3-*a*]carbazole **5a**. Based

Table I — Analytical data of compounds **3a-d, 4a-d** and **6a-d**

Compd	m.p. °C	Yield (%)	Mol.Formula Mol. wt	Found % (Calcd) C	H	N
3a	239-42	80	$C_{17}H_{13}NO_2$ (263.294)	77.55 (77.41	04.97 04.89	05.31 05.50)
3b	228-31	82	$C_{17}H_{13}NO_2$ (263.294)	77.55 (77.50	04.97 04.82	05.31 05.21)
3c	257-60	85	$C_{17}H_{13}NO_2$ (263.294)	77.55 (77.59	04.97 04.91	05.31 05.41)
3d	234-38	79	$C_{16}H_{11}NO_2$ (249.267)	77.09 (77.15	04.44 04.37	05.61 04.57)
4a	192-96	30	$C_{20}H_{14}N_2S$ (314.212)	76.38 (76.42	04.49 04.56	08.91 08.83)
4b	185-89	35	$C_{20}H_{14}N_2S$ (314.212)	76.38 (76.49	04.49 04.38	08.91 08.83)
4c	202-06	30	$C_{20}H_{14}N_2S$ (314.212)	76.38 (76.43	04.49 04.36	08.91 08.83)
4d	193-97	39	$C_{19}H_{12}N_2S$ (300.383)	75.97 (75.85	04.02 04.16	09.32 08.23)
6a	174-77	90	$C_{16}H_{13}NO_3$ (267.282)	71.89 (71.74	04.90 04.89	05.24 05.13)
6b	155-59	86	$C_{16}H_{13}NO_3$ (267.282)	71.89 (71.90	04.90 04.89	05.24 05.19)
6c	188-91	92	$C_{16}H_{13}NO_3$ (267.282)	71.89 (71.71	04.90 04.87	05.24 05.35)
6d	162-66	95	$C_{15}H_{11}NO_3$ (253.255)	71.13 (71.20	04.37 04.40	05.53 05.44)

Table II — ^{1}H NMR data of compounds **3a-d**, **4a-d** and **6a-d**

Compd	^{1}H NMR (δ, ppm)
3a	2.49 (s, 3H, C_7-CH_3), 2.61 (s, 3H, C_2-$COCH_3$), 7.27 (d, 1H, C_8-H, *J*=8.08 Hz), 7.46 (d, 1H, C_9-H, *J*=8.08 Hz), 7.51 (d, 1H, C_4-H, *J*=8.24 Hz), 7.97 (s, 1H, C_6-H), 8.06-8.08 (m, 2H, C_5-H and C_3-H) , 12.11 (b s, 1H, NH)
3b	2.51 (s, 3H, C_8-CH_3), 2.62 (s, 3H, C_2-$COCH_3$), 7.07 (d, 1H, C_7-H, *J*=8.38 Hz), 7.36 (s, 1H, C_9-H), 7.52 (d, 1H, C_6-H, *J*=8.38 Hz), 8.05-8.13 (m, 3H, C_4-H, C_5-H and C_3-H), 12.15 (b s, 1H, NH)
3c	2.63 (s, 3H, C_9-CH_3), 3.32 (s, 3H, C_2-$COCH_3$), 7.14-7.16 (m, 1H, C_7-H), 7.25 (d, 1H, C_8-H, *J* = 8.14 Hz), 7.55 (d, 1H, C_6-H, *J* = 8.14 Hz), 8.02 (d, 1H, C_4-H, *J* = 7.72 Hz), 8.11-8.13 (m, 2H, C_5-H and C_3-H), 12.14 (b s, 1H, NH)
3d	2.62 (s, 3H, C_2-$COCH_3$), 7.23-7.59 (m, 4H, C_6-H, C_7-H, C_8-H and C_9-H), 8.11-8.14 (m, 3H, C_4-H, C_5-H and C_3-H), 12.27 (b s, 1H, NH)
4a	2.54 (s, 3H, C_{10}-CH_3), 7.25-7.98 (m, 9H, aromatic-H), 8.78 (s, 1H, C_6-H), 13.00 (b s, 1H, NH)
4b	2.54 (s, 3H, C_{11}-CH_3), 7.03-8.01 (m, 9H, aromatic-H), 8.58 (s, 1H, C_6-H), 13.02 (b s, 1H, NH)
4c	2.62 (s, 3H, C_{12}-CH_3), 7.16-8.08 (m, 9H, aromatic-H), 8.45 (s, 1H, C_6-H), 13.11 (b s, 1H, NH)
4d	7.40-8.09 (m, 10H, aromatic-H), 8.55 (s, 1H, C_6-H), 13.10 (b s, 1H, NH)
6a	2.50 (m, 3H, C_6-CH_3), 2.51 (m, 3H, C_1-$OCOCH_3$), 7.31-8.01 (m, 5H, aromatic-H), 8.16 (b s, 1H, NH), 10.19 (s, 1H, C_2-CHO)
6b	2.54 (s, 3H, C_7-CH_3), 2.51 (s, 3H,-$OCOCH_3$), 7.08-8.16 (m, 6H, aromatic-5H, and 1 NH), 10.20 (s , 1H, C_2-CHO)
6c	2.57 (s, 3H, C_8-CH_3), 2.59 (s, 3H,-$OCOCH_3$), 7.10-8.04 (m, 6H, aromatic-5H, and NH), 10.21 (s 1H, C_2-CHO)
6d	2.51 (s, 3H, -$OCOCH_3$), 7.22-8.17 (m, 7H, aromatic-6H, and 1NH), 10.19 (s, 1H, C_2-CHO)

on the above discussion and the spectral data, the structure of the product was confirmed to be 1-acetyloxycarbazole-2-carbaldehyde **6a**, which is a simple acylated product. A series of similar compounds **6b-d** were obtained from **2b-d** (**Scheme I, Tables I** and **II**).

Experimental Section

Melting points were determined by Mettler FP-5 apparatus and were uncorrected. The reactions were monitored on TLC. Column chromatographic separations were done using silica gel. IR spectra were recorded in KBr pellets on a Perkin-Elmer model 1600 FT-IR instrument. ^{1}H NMR spectra (400 MHz) were recorded on a Varian AMX 400 spectrometer using TMS as an internal standard. CHN analyses were carried out on a Carlo Erba 1108 model elemental analyzer. Electron impact (EI) mass spectrum was recorded in Jeol (D)-300 EI mass spectrometer. The required precursors 1-hydroxycarbazole-2-carbaldehydes **2** were prepared from 1-hydroxycarbazoles **1** according to our reported procedure[9,13].

Preparation of 1-acetylfuro[2, 3-*a*]carbazoles 3. A mixture consisting of 1-hydroxycarbazole-2-carbaldehyde (**2**, 0.001 mole), chloroacetone (0.001 mole) and K_2CO_3 (1 g) in dry acetone (10 mL) was refluxed for 1 hr on water-bath. Then, the cooled reaction mixture was filtered and washed with excess acetone. This filtrate was then concentrated and poured into ice. The solid separated out was extracted with chloroform, washed with water successively and dried over anhydrous sodium sulphate. The removal of the solvent on evaporation gave the crude product, which was purified by passing through a silica gel column and eluting with petroleum ether-ethyl acetate mixture (95 : 5) to derive the title compound **3**. The physical and spectral data of the series of similar products **3a-d** were compiled in **Tables I** and **II**.

Preparation of benzo[1, 2-*b*]-1,4-thiazepino[2, 3-*a*]carbazoles 4.The appropriate 1-hydroxycarbazole-2-carbaldehyde (**2**, 0.001 mole) was refluxed with *o*-aminothiophenol (0.001 mole) in acetic acid at 140°C for 5 hr. The resulting reaction mixture was then poured into crushed ice. The product separated was extracted with ethylacetate, washed with water and dried over anhydrous sodium sulphate. Excess solvent was removed by evaporation to obtain the crude product which was then purified by passing through a silica gel column and eluting with petroleum ether-ethyl acetate mixture (99:1) to furnish the respective compound **4**. The physical and spectral data of compounds **4a-d** were given in **Tables I** and **II**.

Preparation of 1-acetyloxycarbazole-2-carbaldehydes 6. The respective 1-hydroxycarbazole-2-carbaldehyde (**2,** 0.001mole) was treated with phenylacetic acid (0.001 mole) in acetic anhydride (5 mL) at 120°C for 5 hr. The reaction mixture was poured into crushed ice, extracted with chloroform (3 × 10 mL) and washed with water. The combined organic layers were dried over anhydrous sodium sulphate. Removal

of the solvent yielded the crude product which was purified by column chromatographic technique over silica gel using petroleum ether-ethyl acetate (99 : 1) as a solvent system. The analytical and spectral data of the compounds **5a-d** have been presented in **Tables I** and **II**.

References

1 Katritzky A R & Xie L, *J Org Chem*, 60, **1995,** 3707.
2 Seker M, Vanitha S & Rajendra Prasad K J, *Z Naturforsch*, 49b, **1994,** 687.
3 Rajendra Prasad K J, Vijayalakshmi C S & Sowmithran D, *Org Prep Procedures Int*, 27, **1995,** 686.
4 Sowmithran D & Rajendra Prasad K J, *Heterocycles*, 24, **1986,** 711.
5 Sowmithran D & Rajendra Prasad K J, *Heterocycles*, 24, **1986,** 2197.
6 Sowmithran D & Rajendra Prasad K J, *Indian J Chem*, 25B, **1986,** 1179.
7 Sowmithran D & Rajendra Prasad K J, *Indian J Chem*, 26B, **1987,** 277.
8 Sekar M & Rajendra Prasad K J, *Indian J Chem*, 33B, **1994,** 479.
9 Rajendra Prasad K J & Vijayalakshmi C S, *Indian J Chem*, 33B, **1994,** 481.
10 Pindur U, Haber M & Sattler K, *J Chem Educ*, 70, **1993,** 263.
11 Segall A, Pappa H, Pizzorno M T, Radice M, Amoroso A & Gutkind G, *Il Farmaco,* 51(7), **1996,** 513.
12 Gribble G W, *The Alkaloids Ed*, (Academic Press) 39, **1990,** 239.
13 Shanmugasundaram K & Rajendra Prasad K J, *Heterocycles,* 51, **1999,** 2163.