SYNTHETIC UTILITY OF 1-HYDROXYCARBAZOLE-2-CARBALDEHYDES – SYNTHESES OF FURO-, OXAZINO- AND PYRANOCARBAZOLES

Arputharaj E. MARTIN[1] and Karnam J. RAJENDRA PRASAD[2,*]

Department of Chemistry, Bharathiar University, Coimbatore 641 046, Tamil Nadu, India; e-mail: [1] ebenezermartin@yahoo.com, [2] prasad_125@yahoo.com

Received July 24, 2007
Accepted November 14, 2007

Reaction of 1-hydroxycarbazole-2-carbaldehydes **1** with phenacyl bromide yielded 2-benzoyl-10*H*-furo[2,3-*a*]carbazoles **2**, whereas the reaction with ethyl bromoacetate yielded 1-oxo-1,2-dihydro[1,4]oxazino[2,3,4-*jk*]carbazole-4-carbaldehyde (**4**). The reaction of **1** with ethyl acetoacetate and also with diethyl malonate yielded the pyranocarbazoles **6** and **7**, respectively. All the products were characterized by spectral and analytical means. Plausible mechanisms of product formation are proposed.

Keywords: Carbazoles; Pyranes; Fused heterocycles; Aldehydes; Cyclizations; Furocarbazoles.

Murraya Koenigii[1] is prolific for the source of various carbazole alkaloids like pyrano-, furo-, oxazino- and pyridocarbazoles. The presence of carbazole nucleus in the frame work of various pharmacologically active compounds with anti-tumor[2–4] and anti-HIV[5,6] activities continue to promote their synthetic efforts. Among the carbazoles, some facile precursors such as 2-acetylcarbazol-1-ol[7], 2-benzylidene-2,3,4,9-tetrahydrocarbazol-2-one[8], and reagents like tricarbonyl[(1-5-η)-cyclohexadienylium]iron tetrafluoroborate[9], are available which could be transformed into desired carbazole alkaloids using various reactions. For instance, 2-acetylcarbazol-1-ol[7] is an important synthetic precursor of carbazole alkaloids for obtaining biogenetically possible carbazole alkaloids, These classical synthetic protocols for the synthesis of carbazole alkaloids suffer from some disadvantages such as low yield[7] and lack of easy availability/preparation of the reagent[9], multisteps and harsh reaction conditions[10]. In this connection, we felt that the easily accessible intermediate, 1-hydroxycarbazol-2-carbaldehyde[11–13] reported from our laboratory would make the task much easier to obtain various annulated carbazole alkaloids like furo-, oxazino- and pyranocarbazoles. Earlier workers from our laboratory have reported the synthesis of 2-acetyl-10*H*-furo[2,3-*a*]carbazoles[14]. Keeping this fact in mind, in our present study, we focused our attention on the synthesis of some more oxy-

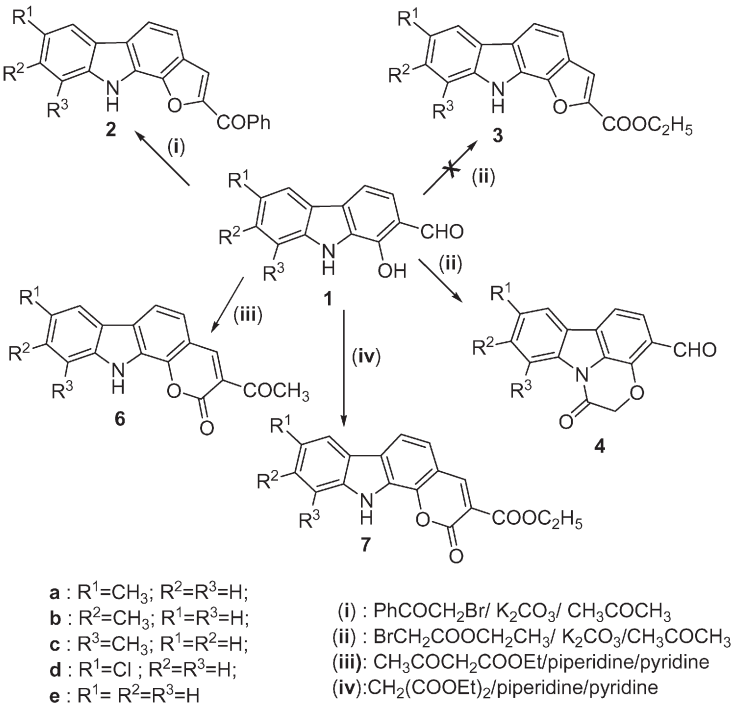
Collect. Czech. Chem. Commun. 2007, Vol. 72, No. 11, pp. 1579–1590

doi:10.1135/cccc20071579

genated fused carbazoles like furo-, oxazino- and pyranocarbazoles with some substituents.

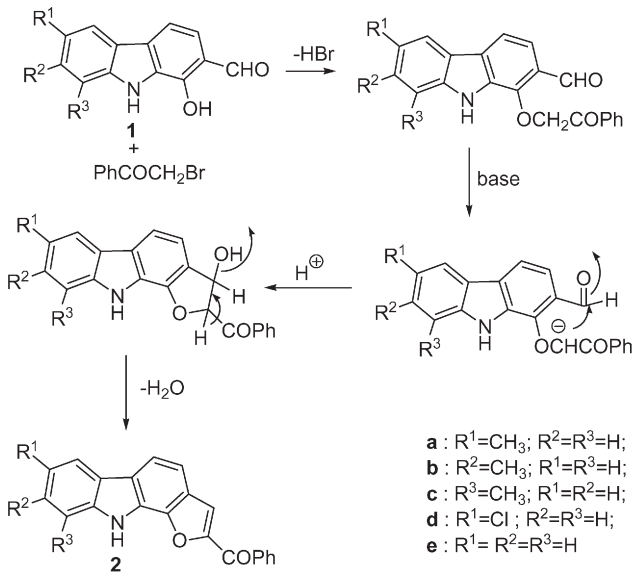
In an anticipation to get 2-benzoyl-10*H*-furo[2,3-*a*]carbazoles **2** from 1-hydroxycarbazole-2-carbaldehydes[11–13] **1**, we treated **1a** with phenacyl bromide[15] and calcined K_2CO_3 in acetone and obtained a crude solid mass, which on purification by column chromatography over silica gel using petroleum ether/ethyl acetate (95:5) gave a yellow powder.

From the spectral and analytical results, the product was characterized as 2-benzoyl-7-methyl-10*H*-furo[2,3-*a*]carbazole (**2a**). The reaction was generalized for other carbazole derivatives **1b**–**1e** (Scheme 1).



SCHEME 1

Mechanistically it may be considered worthwhile that first the *O*-alkylation took place at the C_1-OH group of carbazole. Then the abstraction of an acid proton of C_1-OCH_2COPh by base followed by the carbanionic attack on the aldehyde carbonyl carbon and water elimination yielded the compound **2** (Scheme 2).



SCHEME 2

Earlier it was reported that the reaction of 1-hydroxycarbazole-2-carbaldehyde (**1e**) with ethyl chloroacetate and calcined K_2CO_3 in DMF yielded ethyl 7-methyl-10*H*-furo[2,3-*a*]carbazole-2-carboxylate[12,16] (**3e**). So we have planned to derive the same along with its methyl and chloro substituted derivatives using the reaction of **1** with ethyl bromoacetate. Therefore in another experiment, we treated 1-hydroxycarbazole-2-carbaldehyde derivatives **1** with ethyl bromoacetate and calcined K_2CO_3 in acetone. The reaction of **1a** yielded a crude product, which on purification by column chromatography over silica gel using petroleum ether/ethyl acetate (98:2) gave a pale yellow powder and characterized as 8-methyl-1-oxo-1,2-dihydro[1,4]-oxazino[2,3,4-*jk*]carbazole-4-carbaldehyde (**4a**). Here the reaction ended up with the formation of the unexpected unknown carbazole rather than the expected ethyl 7-methyl-10*H*-furo[2,3-*a*]carbazole-2-carboxylate (**3a**). The reaction was generalized for other carbazole derivatives **1b**, **1d** and **1e** except **1c** (Scheme 1). The support in favour of these unexpected products, 1-oxo-1,2-dihydro[1,4]oxazino[2,3,4-*jk*]carbazole-4-carbaldehydes **4a**, **4b** and **4d**, **4e**, is also obtained from the crystal structure (Fig. 1) of 1-oxo-1,2-dihydro[1,4]oxazino[2,3,4-*jk*]carbazole-4-carbaldehyde[17] (**4e**).

The reaction of 1-hydroxy-8-methylcarbazole-2-carbaldehyde (**1c**) with ethyl bromoacetate under the same condition yielded a white spongy mass after purification by column chromatography. From the spectral results we

have concluded that the product realized was 1-[(ethoxycarbonyl)methoxy]-8-methylcarbazole-2-carbaldehyde (**5c**), which is the possible intermediate in the proposed mechanism of the conversion of **1** into **4** (Scheme 3). In order to cyclize 1-[(ethoxycarbonyl)methoxy]-8-methylcarbazole-2-carbaldehyde (**5c**), we carried out the reaction of 1-hydroxy-8-methylcarbazole-2-carbaldehyde (**1c**) with ethyl acetoacetate in DMF/K_2CO_3. Here we have also realized the same compound 1-[(ethoxycarbonyl)methoxy]-8-methylcarbazole-2-carbaldehyde (**5c**), rather than the expected cyclized product.

The plausible mechanism for the formation of compound **4** has been proposed (Scheme 3). In the formation of compounds **4a**, **4b** and **4d**, **4e**, the initial attack of a lone electron pair on the oxygen of the C_1-OH at the methylene carbon of the $BrCH_2$ group of ethyl bromoacetate is assumed, followed by HBr elimination producing *O*-alkylated product **5.** Then the lone electron pair on the carbazole NH group again attacks the ester carbonyl group of C_1-$OCH_2COOCH_2CH_3$ to give intermediate **I** as we observed in the previous case. After that the intermediate **I** on prototropic shift followed by elimination of ethanol produces the respective products. Here we can conclude that in the previous case the elimination of water molecule is effected due to extended conjugation with phenyl group whereas here there is no extended conjugation available to promote the elimination of water molecule rather than the ethanol molecule. In the case of **1c**, the compound **5c** has been a product, instead of either of the cyclized products (expected/realized). It has been concluded that the methyl group at C_8 position restricted the approach of C_1-$OCH_2COOCH_2CH_3$ to the carbazole NH group and further cyclization was prevented. Also the K_2CO_3 in

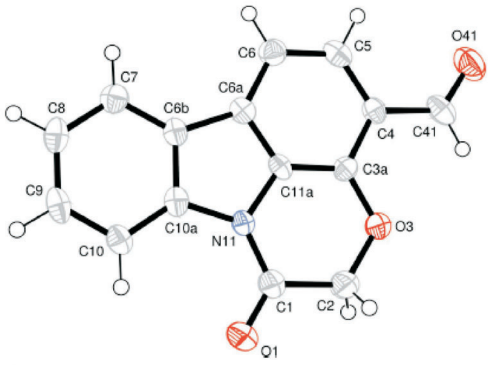
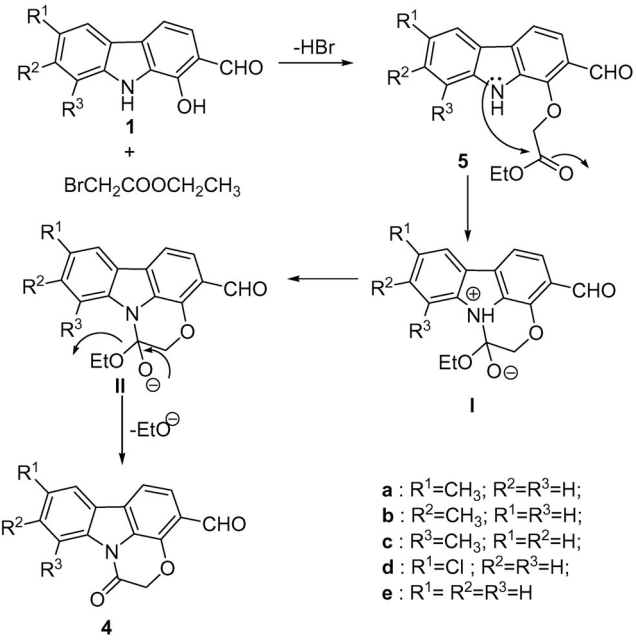


FIG. 1
ORTEP drawing of crystal structure of **4a**

acetone/DMF is not basic enough to abstract the acid proton at C_1 (C_1-OC*H*$_2$COOCH$_2$CH$_3$), thus stopping the reaction at this stage, to give **5c**.

We have also attempted the synthesis of pyranocarbazoles. For that we treated 1-hydroxycarbazole-2-carbaldehydes **1** with ethyl acetoacetate and diethyl malonate. When 1-hydroxy-6-methylcarbazole-2-carbaldehyde (**1a**) reacted with ethyl acetoacetate in pyridine and a catalytic amount of piperidine, yielded a yellow solid mass. From the spectral and analytical results, its structure was assigned as 3-acetyl-8-methyl-2,11-dihydropyrano-[2,3-*a*]carbazol-2-one (**6a**) .



In the case of **1c** reaction stops afer the first step due to steric crowding

SCHEME 3

When the same type of the reaction was extended to diethyl malonate, **1a** yielded a yellow solid mass. All the spectral and analytical details confirm the product as ethyl 8-methyl-2-oxo-2,11-dihydropyrano[2,3-*a*]carbazole-3-carboxylate (**7a**).

A plausible mechanism for the formation of compounds **6** and **7** is proposed. Initially the lone electron pair on the hydroxy group of **1** attacks the carbonyl carbon of the ester group of both the active methylene compounds, ethyl acetoacetate and diethyl malonate to give the respective

O-alkylated products by elimination of ethanol molecule. Then the base abstracts the highly acid proton at C-1 followed by the intramolecular attack of the carbanion on the aldehyde carbonyl carbon at C-2 and water elimination yielded the respective products **6** and **7.**

In conclusion, the reaction of 1-hydroxycarbazole-2-carbaldehyde (**1e**) and its derivatives substituted at C-6, C-7 and C-8 with phenacyl bromide led to the formation of novel 2-benzoyl-10*H*-furo[2,3-*a*]carbazoles **2**. The reaction of hydroxy aldehydes **1** with ethyl bromoacetate yielded the novel 1-oxo-1,2-dihydro[1,4]oxazino[2,3,4-*jk*]carbazole-4-carbaldehydes **4** provided that the ring carbon atom C-8 was not substituted. The attempts to synthesize pyranocarbazoles were successful yielding the pyrano[2,3-*a*]carbazoles **6** and **7**.

EXPERIMENTAL

Melting points were determined with a Mettler FP 51 apparatus (Mettler Instruments, Switzerland) and were uncorrected. IR spectra (ν_{max}, cm^{-1}) were recorded using KBr on a Shimadzu FTIR-8201PC spectrophotometer (Shimadzu, Japan). NMR spectra (δ, ppm; *J*, Hz) were recorded in $CDCl_3$ or DMSO-d_6 on a Varian AMX 400 FT-NMR (Varian Australia, Australia) using TMS as internal standard. Mass spectra were recorded on a Jeol-JMS-D-300 mass spectrometer (70 eV; Jeol, Japan). Microanalyses were done on a Vario EL III Model CHNS analyzer (Vario, Germany). The purity of the products was tested by TLC using glass plates coated with silica gel G (Hi Media Laboratories, India) and petroleum ether/ethyl acetate (85:15). Phenacyl bromide has been prepared by bromination[15] of acetophenone (Hi Media Laboratories, India). Ethyl bromoacetate was purchased from Loba Chemie India Ltd.

2-Benzoyl-10*H*-furo[2,3-*a*]carbazoles **2a**–**2e**. General Procedure

A mixture of the respective 1-hydroxycarbazole-2-carbaldehyde **1** (0.001 mol), phenacyl bromide (200 mg, 0.001 mol) and calcined potassium carbonate (276 mg, 0.002 mol) in dry acetone (15 ml) was refluxed on a steam bath for 3 h. The reaction was monitored by TLC. After completion of the reaction the solvent was removed and the reaction mixture was poured into ice water. The solid was filtered off, washed with water and dried. Then it was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (95:5) as eluant, after removal of the solvent the respective 2-benzoyl-10*H*-furo[2,3-*a*]carbazole **3** was obtained.

2-Benzoyl-7-methyl-10H-furo[2,3-a]carbazole (**2a**): Yellow amorphous powder, m.p. 170–172 °C. Yield 62%. For $C_{22}H_{15}NO_2$ (325.4) calculated: 81.21% C, 4.65% H, 4.30% N; found: 81.25% C, 4.62% H, 4.34% N. IR: 2922, 2856, 1688, 1630, 968. ^{1}H NMR (400 MHz, DMSO-d_6): 12.21 b s, 1 H (H-10, deuterium-exchangeable); 8.13–7.98 m, 3 H (H-4, H-5, H-2′); 7.99 s, 1 H (H-3); 7.96 s, 1 H (H-6); 7.78–7.60 m, 3 H (H-3′, H-5′, H-6′); 7.57–7.52 d, 1 H, *J*(8,9) = 8.30 (H-8); 7.50–7.45 d, 1 H, *J*(9,8) = 8.30 (H-9); 7.34–7.24 m, 1 H (H-4′); 2.45 s, 3 H (CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): 189.7 (COPh); 136.2 (C-2); 127.5 (C-3); 139.9 (C-10b); 130.8 (C-10a); 130.1 (C-9a); 129.4 (C-5a); 128.1 (C-5b); 126.9 (C-1′); 126.8 (C-2′, C-6′); 123.2 (C-3′, C-5′); 120.9 (C-4′); 119.9 (C-7); 118.7 (C-8); 118.1 (C-6); 117.1 (C-9); 116.3 (C-4); 113.7 (C-5);

110.4 (C-3a); 19.3 (CH_3). MS (EI, 70 eV), *m/z* (rel.%): 325 (64) [M^+]; 324 (100); 311 (28); 296 (60); 270 (22); 198 (25).

2-Benzoyl-8-methyl-10H-furo[2,3-a]carbazole (**2b**): Yellow amorphous powder, m.p. 164–166 °C. Yield 58%. For $C_{22}H_{15}NO_2$ (325.4) calculated: 81.21% C, 4.65% H, 4.30% N; found: 81.18% C, 4.61% H, 4.37% N. IR: 2921, 2850, 1692, 1636, 969. ^{1}H NMR (400 MHz, DMSO-d_6): 12.22 b s, 1 H (H-10, deuterium-exchangeable); 8.20–7.07 m, 10 H (H-4, H-5, H-6, H-7, H-9, H-2′, H-3′, H-4′, H-5′, H-6′); 7.93 s, 1 H (H-3); 2.52 s, 3 H (CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): 190.0 (COPh); 137.2 (C-2); 127.2 (C-3); 140.4 (C-10b); 131.1 (C-10a); 130.2 (C-9a); 129.8 (C-5a); 128.0 (C-5b); 126.4 (C-1′); 125.0 (C-2′, C-6′); 123.2 (C-8); 121.0 (C-4′); 119.8 (C-3′, C-5′); 118.2 (C-7); 116.7 (C-6); 116.1 (C-9); 114.3 (C-4); 112.4 (C-5); 109.7 (C-3a); 19.3 (CH_3). MS (EI, 70 eV), *m/z* (rel.%): 325 (62) [M^+]; 324 (100); 311 (34); 296 (56); 270 (28); 198 (20).

2-Benzoyl-9-methyl-10H-furo[2,3-a]carbazole (**2c**): Yellow amorphous powder, m.p. 174–176 °C. Yield 66%. For $C_{22}H_{15}NO_2$ (325.4) calculated: 81.21% C, 4.65% H, 4.30% N; found: 81.16% C, 4.66% H, 4.30% N. IR: 2922, 2856, 1696, 1622, 1331, 964. ^{1}H NMR (400 MHz, DMSO-d_6): 12.23 b s, 1 H (H-10, deuterium-exchangeable); 8.15–8.10 d, 1 H, *J*(5,4) = 8.30 (H-5); 8.09–7.94 m, 3 H (H-2′, H-5′, H-6′); 7.97 s, 1 H (H-3); 7.79–7.61 m, 3 H (H-6, H-7, H-8); 7.60–7.54 d, 1 H, *J*(4,5) = 8.30 (H-4); 7.28–7.22 m, 1 H (H-3′); 7.19–7.13 t, 1 H, *J*(4′,3′,5′) = 7.4 (H-4′); 2.64 s, 3 H (CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): 190.4 (COPh); 136.4 (C-2); 126.0 (C-3); 140.4 (C-10b); 132.0 (C-10a); 130.6 (C-9a); 129.9 (C-5a); 129.0 (C-5b); 127.7 (C-1′); 125.4 (C-2′, C-6′); 122.9 (C-3′, C-5′); 121.4 (C-4′); 120.0 (C-9); 118.9 (C-7); 117.2 (C-8); 116.9 (C-6); 115.2 (C-4); 113.4 (C-5); 110.0 (C-3a); 19.9 (CH_3). MS (EI, 70 eV), *m/z* (rel.%): 325 (60) [M^+]; 324 (100); 311 (32); 296 (50); 270 (18); 199 (12); 198 (22).

2-Benzoyl-7-chloro-10H-furo[2,3-a]carbazole (**2d**): Yellow amorphous powder, m.p. 145–147 °C. Yield 54%. For $C_{21}H_{12}ClNO_2$ (345.8) calculated: 72.97% C, 3.50% H, 4.05% N; found: 72.77% C, 3.53% H, 4.03% N. IR: 2924, 2855, 1688, 1629, 1577, 976. ^{1}H NMR (400 MHz, DMSO-d_6): 12.54 b s, 1 H (H-10, deuterium-exchangeable); 8.35–8.31 d, 1 H, *J*(6,8) = 1.96 (H-6); 8.21–8.17 d, 1 H, *J*(5,4) = 8.40 (H-5); 8.09–8.03 m, 2 H (H-4, H-9); 7.98 s, 1 H (H-3); 7.78–7.56 m, 5 H (H-2′, H-3′, H-4′, H-5′, H-6′); 7.48–7.43 dd, 1 H *J*(8,9) = 8.6, *J*(8,6) = 1.96 (H-8). ^{13}C NMR (100 MHz, DMSO-d_6): 190.1 (COPh); 136.4 (C-2); 126.1 (C-3); 141.0 (C-10b); 138.7 (C-10a); 136.0 (C-7); 130.4 (C-9a); 129.4 (C-5a); 127.7 (C-5b); 124.6 (C-1′); 121.9 (C-2′, C-6′); 120.7 (C-3a); 119.0 (C-3′, C-5′); 117.0 (C-4′); 116.1 (C-8); 115.1 (C-6); 114.7 (C-9); 113.1 (C-4); 109.4 (C-5). MS (EI, 70 eV), *m/z* (rel.%): 345 (62) [M^+]; 347 (28) [M^{2+}]; 316 (50); 309 (27).

2-Benzoyl-10H-furo[2,3-a]carbazole (**2e**): Yellow amorphous powder, m.p. 164–166 °C. Yield 64%. For $C_{21}H_{13}NO_2$ (311.3) calculated: 81.01% C, 4.21% H, 4.50% N; found: 81.07% C, 4.18% H, 4.47% N. IR: 2924, 2850, 1626, 1332, 970. ^{1}H NMR (400 MHz, DMSO-d_6): 12.35 b s, 1 H (H-10, deuterium-exchangeable); 8.25–7.20 m, 11 H (H-4, H-5, H-6, H-7, H-8, H-9, H-2′, H-3′, H-4′, H-5′, H-6′); 7.97 s, 1 H (H-3). ^{13}C NMR (100 MHz, DMSO-d_6): 190.4 (COPh); 135.6 (C-2); 126.1 (C-3); 139.0 (C-10b); 132.1 (C-10a); 130.1 (C-9a); 129.4 (C-5a); 126.9 (C-5b); 124.6 (C-1′); 121.7 (C-2′, C-6′); 120.4 (C-3′, C-5′); 118.4 (C-4′); 117.9 (C-7); 117.1 (C-8); 116.9 (C-6); 116.0 (C-9); 114.4 (C-4); 113.2 (C-5); 110.1 (C-3a). MS (EI, 70 eV), *m/z* (rel.%): 311 (70) [M^+]; 310 (100); 296 (27); 282 (62); 256 (22); 185 (20); 184 (20).

Reaction of 1-Hydroxycarbazole-2-carbaldehydes **1a**–**1e** with Ethyl Bromoacetate. General Procedure

A mixture of the respective 1-hydroxycarbazole-2-carbaldehyde **1** (0.001 mol), ethyl bromoacetate (166 mg, 0.001 mol) and calcined potassium carbonate (276 mg, 0.002 mol) in dry acetone (15 ml) was refluxed in a steam bath for 3 h. The reaction was monitored by TLC. After completion of the reaction the solvent was removed and the mixture was poured into ice water. The solid was filtered off, washed with water and dried. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (95:5) as eluant to give the respective product **4**. In the case of **1c**, the product **5c** is obtained instead of **4c**.

8-Methyl-1-oxo-1,2-dihydro[1,4]oxazino[2,3,4-jk]carbazole-4-carbaldehyde (**4a**): Pale yellow amorphous powder, m.p. 145–147 °C. Yield 52%. For $C_{16}H_{11}NO_3$ (265.3) calculated: 72.45% C, 4.18% H, 5.28% N; found: 72.40% C, 4.20% H, 5.23% N. IR: 2921, 2850, 1712, 1665, 1453. ^{1}H NMR (400 MHz, $CDCl_3$): 10.29 s, 1 H (CHO); 8.12–8.11 d, 1 H, *J*(6,5) = 8.2 (H-6); 8.06 s, 1 H (H-7); 7.78–7.72 d, 1 H, *J*(10,9) = 8.1 (H-10); 7.69–7.63 d, 1 H, *J*(9,10) = 8.1 (H-9); 7.51–7.47 d, 1 H, *J*(5,4) = 8.2 (H-5); 5.24 s, 2 H (H-2); 2.49 s, 3 H (CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): 195.7 (CHO); 173.4 (C-1); 139.4, 137.4, 136.4, 128.6, 122.1, 120.5, 119.2, 118.1, 117.4, 116.6, 113.4, 110.1 (12 arom. C); 67.3 (C-2); 19.3 (CH_3). MS (EI, 70 eV), *m/z* (rel.%): 265 (43) [M^+]; 264 (20); 236 (100); 194 (23); 180 (21); 164 (32).

9-Methyl-1-oxo-1,2-dihydro[1,4]oxazino[2,3,4-jk]carbazole-4-carbaldehyde (**4b**): Pale yellow amorphous powder, m.p. 152–154 °C. Yield 48%. For $C_{16}H_{11}NO_3$ (265.3) calculated: 72.45% C, 4.18% H, 5.28% N; found: 72.41% C, 4.16% H, 5.26% N. IR: 2922, 2856, 1708, 1668, 1642, 1451. ^{1}H NMR (400 MHz, $CDCl_3$): 10.40 s, 1 H (CHO); 8.24 s, 1 H (H-10); 7.92–7.86 d, 1 H, *J*(6,5) = 7.9 (H-6); 7.81–7.76 d, 1 H, *J*(7,8) = 8.1 (H-7); 7.58–7.52 d, 1 H, *J*(8,7) = 8.1 (H-8); 7.36–7.30 d, 1 H, *J*(5,6) = 7.9 (H-5); 5.16 s, 2 H (H-2); 2.58 s, 3 H (CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): 196.4 (CHO); 171.7 (C-1); 140.3, 137.9, 137.2, 128.7, 122.1, 120.3, 119.5, 118.7, 118.1, 116.7, 113.3, 110.4 (12 arom. C); 67.6 (C-2); 19.2 (CH_3). MS (EI, 70 eV), *m/z* (rel.%): 265 (48) [M^+]; 264 (29); 236 (100); 194 (16); 180 (18); 164 (40).

1-[(Ethoxycarbonyl)methoxy]-8-methylcarbazole-2-carbaldehyde (**5c**): White spongy mass, m.p. 166–168 °C. Yield 68%. For $C_{18}H_{17}NO_4$ (311.3) calculated: 69.44% C, 5.50% H, 4.50% N; found: 69.58% C, 5.47% H, 4.52% N. IR: 3285, 2921, 2850, 1764, 1658, 1450. ^{1}H NMR (400 MHz, $CDCl_3$): 10.40 s, 1 H (CHO); 10.03 b s, 1 H (H-9); 7.98–7.90 m, 2 H (H-4, H-5); 7.68–7.62 d, 1 H, *J*(3,4) = 8.1 (H-3); 7.34–7.30 d, 1 H, *J*(7,6) = 8.1 (H-7); 7.21–7.15 m, 1 H (H-6); 4.85 s, 2 H ($OC\mathbf{H}_2COOCH_2CH_3$); 4.35–4.26 q, 2 H, *J* = 7.1 ($OCH_2COOC\mathbf{H}_2CH_3$); 2.65 s, 3 H ($CH_3$); 1.36–1.27 t, 3 H, *J* = 7.1 ($OCH_2COOCH_2C\mathbf{H}_3$). ^{13}C NMR (100 MHz, $CDCl_3$): 197.5 (CHO); 173.2 ($OCH_2\mathbf{C}OOCH_2CH_3$); 140.0, 138.1, 137.0, 128.0, 121.1, 120.2, 119.1, 118.0, 117.4, 116.4, 112.9, 111.2 (12 arom. C); 68.4 ($O\mathbf{C}H_2COOCH_2CH_3$); 64.3 ($OCH_2COO\mathbf{C}H_2CH_3$); 20.1 ($CH_3$); 19.5 ($OCH_2COOCH_2\mathbf{C}H_3$). MS (EI, 70 eV), *m/z* (rel.%): 311 (36) [M^+]; 282 (44); 266 (100); 264 (12); 236 (98); 198 (32).

8-Chloro-1-oxo-1,2-dihydro[1,4]oxazino[2,3,4-jk]carbazole-4-carbaldehyde (**4d**): Pale yellow amorphous powder, m.p. 163–165 °C. Yield 50%. For $C_{15}H_8ClNO_3$ (285.7) calculated: 63.06% C, 2.82% H, 4.90% N; found: 62.89% C, 2.84% H, 4.90% N. IR: 2923, 2885, 1716, 1682, 1643, 1445. ^{1}H NMR (400 MHz, $CDCl_3$): 10.42 s, 1 H (CHO); 8.36–8.32 d, 1 H, *J*(6,5) = 8.2 (H-6); 8.01–7.98 d, 1 H, *J*(7,9) = 1.9 (H-7); 7.84–7.79 d, 1 H, *J*(10,9) = 8.2 (H-10); 7.61–7.55 m, 2 H (H-5, H-9); 5.18 s, 2 H (H-2). ^{13}C NMR (100 MHz, $CDCl_3$): 198.3 (CHO); 174.1 (C-1); 140.7, 139.4, 137.8, 129.9, 121.8, 120.5, 119.7, 118.8, 117.8, 114.7, 112.4, 110.6

(12 arom. C); 67.4 (C-2). MS (EI, 70 eV), *m/z* (rel.%): 285 (40) [M^+]; 287 (12) [M^{2+}]; 284 (20); 256 (100); 251 (22); 214 (26).

1-Oxo-1,2-dihydro[1,4]oxazino[2,3,4-jk]carbazole-4-carbaldehyde (**4e**): Pale yellow crystals, m.p. 160–162 °C. Yield 50%. For $C_{15}H_9NO_3$ (251.2) calculated: 71.71% C, 3.61% H, 5.58% N; found: 71.81% C, 3.63% H, 5.56% N. IR: 2924, 2857, 1693, 1642, 1445. ^{1}H NMR (400 MHz, $CDCl_3$): 10.41 s, 1 H (CHO); 8.44–8.37 d, 1 H, *J*(6,5) = 8.2 (H-6); 8.05–8.01 d, 1 H, H-10, *J*(10,9) = 7.8 (H-10); 7.84–7.79 d, 1 H, *J*(5,6) = 8.2 (H-5); 7.67–7.63 m, 1 H (H-9); 7.63–7.58 d, 1 H, *J*(7,8) = 8.2 (H-7); 7.53–7.49 m, 1 H (H-8); 5.17 s, 2 H (H-2). ^{13}C NMR (100 MHz, $CDCl_3$): 198.1 (CHO); 169.4 (C-1); 139.9, 137.4, 130.1, 129.7, 121.3, 120.6, 119.2, 118.6, 118.0, 114.4, 112.8, 109.9 (12 arom. C); 67.1 (C-2). MS (EI, 70 eV), *m/z* (rel.%): 251 (37) [M^+]; 250 (26); 222 (100); 180 (20); 179 (11).

3-Acetyl-2,11-dihydropyrano[2,3-*a*]carbazol-2-ones **6a**–**6e**.
General Procedure

A mixture of the respective 1-hydroxycarbazole-2-carbaldehyde **1** (0.001 mol), ethyl acetoacetate (0.2 ml, 0.001 mol) in dry pyridine (20 ml) was heated to 50–60 °C on an oil bath. Then piperidine (3–4 drops) was added dropwise and the mixture was refluxed for 2 h. The reaction was monitored by TLC. After completion of the reaction the reaction mixture was neutralized with cold aqueous HCl and poured into ice water. The solid was filtered off, washed with water and dried. Then it was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (80:20) as eluant to give the respective product.

3-Acetyl-8-methyl-2,11-dihydropyrano[2,3-a]carbazol-2-one (**6a**): Yellow amorphous powder, m.p. 210–212 °C. Yield 52%. For $C_{18}H_{13}NO_3$ (291.3) calculated: 74.22% C, 4.50% H, 4.81% N; found: 74.12% C, 4.54% H, 4.77% N. IR: 3302, 2920, 1709, 1670, 1586. ^{1}H NMR (400 MHz, DMSO-d_6): 12.27 b s, 1 H (H-11, deuterium-exchangeable); 8.84 s, 1 H (H-4); 8.13–8.07 d, 1 H, *J*(6,5) = 8.2 (H-6); 8.02 s, 1 H (H-7); 7.65–7.59 d, 1 H, *J*(5,6) = 8.2 (H-5); 7.50–7.44 d, 1 H, *J*(10,9) = 8.40 (H-10); 7.38–7.30 d, 1 H, *J*(9,10) = 8.40 (H-9); 2.62 s, 3 H ($COCH_3$); 2.48 s, 3 H (CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): 198.7 ($COCH_3$); 166.2 (C-2); 137.4 (C-4); 134.4 (C-3); 136.9, 136.1, 131.3, 130.5, 130.0, 129.1, 122.5, 121.7, 117.8, 114.7, 112.4, 110.6 (12 arom. C); 25.9 ($COCH_3$); 19.0 (CH_3). MS (EI, 70 eV), *m/z* (rel.%): 291 (64) [M^+]; 276 (45); 262 (100); 248 (32); 244 (22); 217 (39); 196 (23).

3-Acetyl-9-methyl-2,11-dihydropyrano[2,3-a]carbazol-2-one (**6b**): Yellow amorphous powder, m.p. 198–199 °C. Yield 55%. For $C_{18}H_{13}NO_3$ (291.3) calculated: 74.22% C, 4.50% H, 4.81% N; found: 74.29% C, 4.57% H, 4.83% N. IR: 3323, 2923, 1717, 1673, 1587. ^{1}H NMR (400 MHz, DMSO-d_6): 12.24 b s, 1 H (H-11, deuterium-exchangeable); 8.86 s, 1 H (H-4); 8.10–8.04 d, 1 H, *J*(6,5) = 8.0 (H-6); 7.64–7.59 d, 1 H, *J*(5,6) = 8.0 (H-5); 7.42 s, 1 H (H-10); 7.14–7.01 m, 2 H (H-7, H-8); 2.83 s, 3 H ($COCH_3$); 2.63 s, 3 H (CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): 197.2 ($COCH_3$); 162.9 (C-2); 139.2 (C-4); 135.1 (C-3); 138.6, 137.9, 134.3, 131.8, 129.8, 129.1, 124.5, 121.9, 119.8, 118.2, 112.9, 111.7 (12 arom. C); 26.6 ($COCH_3$); 21.0 (CH_3). MS (EI, 70 eV), *m/z* (rel.%): 291 (55) [M^+]; 276 (31); 262 (100); 248 (38); 244 (22); 224 (20); 217 (45); 196 (18).

3-Acetyl-10-methyl-2,11-dihydropyrano[2,3-a]carbazol-2-one (**6c**): Yellow amorphous powder, m.p. 215–217 °C. Yield 52%. For $C_{18}H_{13}NO_3$ (291.3) calculated: 74.22% C, 4.50% H, 4.81% N; found: 74.31% C, 4.44% H, 4.73% N. IR: 3332, 2923, 1720, 1670, 1585. ^{1}H NMR (400 MHz, DMSO-d_6): 12.29 b s, 1 H (H-11, deuterium-exchangeable); 8.75 s, 1 H (H-4); 8.01–7.93 m, 2 H (H-5, H-6); 7.47–7.43 d, 1 H, *J*(7,8) = 8.2 (H-7); 7.39–7.35 d, 1 H, *J*(9,8) = 8.0 (H-9);

7.29–7.20 m, 1 H (H-8); 2.78 s, 3 H ($COCH_3$); 2.64 s, 3 H (CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): 199.7 ($COCH_3$); 161.0 (C-2); 140.2 (C-4); 135.4 (C-3); 138.1, 137.1, 133.8, 132.0, 129.1, 126.5, 124.4, 120.9, 118.8, 118.0, 114.3, 106.4 (12 arom. C); 23.9 ($COCH_3$); 21.7 (CH_3). MS (EI, 70 eV), *m/z* (rel.%): 291 (72) [M^+]; 276 (40); 262 (100); 248 (25); 244 (20); 217 (45).

3-Acetyl-8-chloro-2,11-dihydropyrano[2,3-a]carbazol-2-one (**6d**): Yellow amorphous powder, m.p. 222–224 °C. Yield 60%. For $C_{17}H_{10}ClNO_3$ (311.7) calculated: 65.50% C, 3.23% H, 4.49% N; found: 65.84% C, 3.20% H, 4.55% N. IR: 3322, 2925, 1728, 1653, 1586. ^1H NMR (400 MHz, DMSO-d_6): 12.34 b s, 1 H (H-11, deuterium-exchangeable); 8.80 s, 1 H (H-4); 8.32 s, 1 H (H-7); 8.22–8.16 d, 1 H, *J*(6,5) = 8.5 (H-6); 7.63–7.57 d, 1 H, *J*(5,6) = 8.5 (H-5); 7.44–7.32 m, 2 H (H-9, H-10); 2.63 s, 3 H ($COCH_3$). ^{13}C NMR (100 MHz, DMSO-d_6): 199.8 ($COCH_3$); 162.2 (C-2); 139.4 (C-4); 133.7 (C-3); 141.9, 137.8, 134.8, 132.6, 131.1, 128.3, 124.9, 120.7, 116.8, 113.9, 111.4, 107.4 (12 arom. C); 27.9 ($COCH_3$). MS (EI, 70 eV), *m/z* (rel.%): 311 (100) [M^+]; 313 (38); 282 (78); 268 (45); 264 (32); 237 (20); 216 (18).

3-Acetyl-2,11-dihydropyrano[2,3-a]carbazol-2-one (**6e**): Yellow amorphous powder, m.p. 187–189 °C. Yield 58%. For $C_{17}H_{11}NO_3$ (277.3) calculated: 73.64% C, 4.00% H, 5.05% N; found: 73.91% C, 3.97% H, 5.10% N. IR: 3295, 2920, 1715, 1674, 1588. ^1H NMR (400 MHz, DMSO-d_6): 12.37 b s, 1 H (H-11, deuterium-exchangeable); 8.84 s, 1 H (H-4); 8.27–8.21 d, 1 H, *J*(10,9) = 7.8 (H-10); 8.17–8.12 d, 1 H, *J*(6,5) = 8.1 (H-6); 7.69–7.64 d, 1 H, *J*(7,6) = 8.2 (H-5); 7.61–7.56 d, 1 H, *J*(5,6) = 8.2 (H-5); 7.55–7.49 m, 1 H (H-8); 7.30–7.23 m, 1 H (H-9); 2.68 s, 3 H ($COCH_3$). ^{13}C NMR (100 MHz, DMSO-d_6): 200.7 ($COCH_3$); 167.0 (C-2); 139.4 (C-4); 138.4 (C-3); 136.7, 134.3, 131.3, 130.5, 129.9, 127.5, 122.2, 121.0, 118.8, 114.3, 111.7, 109.0 (12 arom. C); 25.9 ($COCH_3$). MS (EI, 70 eV), *m/z* (rel.%): 277 (60) [M^+]; 262 (45); 248 (100); 230 (35); 203 (27); 182 (30).

Ethyl 2-Oxo-2,11-dihydropyrano[2,3-*a*]carbazole-3-carboxylates **7a**–**7e**.
General Procedure

A mixture of respective 1-hydroxycarbazole-2-carbaldehyde **1** (0.001 mol), diethyl malonate (0.2 ml, 0.001 mol) in dry pyridine (20 ml) was heated to 50–60 °C in an oil bath. Then piperidine (3–4 drops) was added dropwise and the mixture was refluxed for 2 h. The reaction was monitored by TLC. After completion of the reaction the reaction mixture was neutralized using cold aqueous HCl and poured into ice water. The solid was filtered off, washed with water and dried. Then it was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (80:20) as eluant.

Ethyl 8-methyl-2-oxo-2,11-dihydropyrano[2,3-a]carbazole-3-carboxylate (**7a**): Yellow amorphous powder, m.p. 246–248 °C. Yield 64%. For $C_{19}H_{15}NO_4$ (321.3) calculated: 71.02% C, 4.71% H, 4.36% N; found: 71.12% C, 4.64% H, 4.30% N. IR: 3289, 2921, 1731, 1645, 1294. ^1H NMR (400 MHz, DMSO-d_6): 12.34 b s, 1 H (H-11, deuterium-exchangeable); 8.90 s, 1 H (H-4); 8.08 s, 1 H (H-7); 7.95–7.90 d, 1 H, *J*(6,5) = 8.1 (H-6); 7.50–7.45 d, 1 H, *J*(10,9) = 8.1 (H-10); 7.40–7.34 d, 1 H, *J*(9,10) = 8.4 (H-9); 7.33–7.27 d, 1 H, *J*(5,6) = 8.1 (H-5); 4.26–4.16 q, 2 H, *J* = 7.2 ($COOCH_2CH_3$); 2.55 s, 3 H (CH_3); 1.34–1.22 t, 3 H, *J* = 7.2 ($COOCH_2CH_3$). ^{13}C NMR (100 MHz, DMSO-d_6): 170.3 (COOEt); 157.7 (C-2); 140.4 (C-4); 117.3 (C-3); 135.3, 133.9, 132.7, 127.4, 124.0, 120.9, 120.0, 118.7, 115.8, 114.1, 110.4, 107.6 (12 arom. C); 59.3 ($COOCH_2CH_3$); 21.9 (CH_3); 15.4 ($COOCH_2CH_3$). MS (EI, 70 eV), *m/z* (rel.%): 321 (100) [M^+]; 276 (45); 262 (98); 248 (32); 244 (22); 217 (39); 196 (23).

Ethyl 9-methyl-2-oxo-2,11-dihydropyrano[2,3-a]carbazole-3-carboxylate (**7b**): Yellow amorphous powder, m.p. 218–220 °C. Yield 60%. For $C_{19}H_{15}NO_4$ (321.3) calculated: 71.02% C, 4.71% H, 4.36% N; found: 71.18% C, 4.68% H, 4.39% N. IR: 3354, 2923, 1730, 1652, 1285. ^{1}H NMR (400 MHz, DMSO-d_6): 12.21 b s, 1 H (H-11, deuterium-exchangeable); 8.92 s, 1 H (H-4); 8.14–8.03 m, 2 H (H-5, H-6); 7.67–7.56 m, 2 H (H-7, H-8); 7.42 s, 1 H (H-10); 4.35–4.27 q, 2 H, *J* = 7.1 (COOC**H**$_2$CH$_3$); 2.83 s, 3 H (CH$_3$); 1.37–1.29 t, 3 H, *J* = 7.1 (COOCH$_2$C**H**$_3$). ^{13}C NMR (100 MHz, DMSO-d_6): 168.0 (**C**OOEt); 154.1 (C-2); 141.2 (C-4); 116.9 (C-3); 134.7, 132.1, 130.8, 129.1, 125.6, 119.9, 1118.7, 116.4, 115.8, 114.4, 108.9, 104.3 (12 arom. C); 60.1 (COO**C**H$_2$CH$_3$); 19.7 (CH$_3$); 16.1 (COOCH$_2$**C**H$_3$). MS (EI, 70 eV), *m/z* (rel.%): 321 (100) [M$^+$]; 276 (40); 262 (90); 248 (50); 244 (21); 217 (22).

Ethyl 10-methyl-2-oxo-2,11-dihydropyrano[2,3-a]carbazole-3-carboxylate (**7c**): Yellow amorphous powder, m.p. 197–199 °C. Yield 52%. For $C_{19}H_{15}NO_4$ (321.3) calculated: 71.02% C, 4.71% H, 4.36% N; found: 70.87% C, 4.76% H, 4.31% N. IR: 3231, 2928, 1717, 1611, 1266. ^{1}H NMR (400 MHz, DMSO-d_6): 12.24 b s, 1 H (H-11, deuterium-exchangeable); 8.79 s, 1 H (H-4); 8.01–7.90 m, 2 H (H-6, H-7); 7.58–7.55 m, 1 H (H-8); 7.44–7.40 d, 1 H, *J*(5,6) = 8.2 (H-5); 7.38–7.34 d, 1 H, *J*(9,10) = 8.0 (H-9); 4.50–4.43 q, 2 H, *J* = 7.1 (COOC**H**$_2$CH$_3$); 2.63 s, 3 H (CH$_3$); 1.49–1.43 t, 3 H, *J* = 7.1 (COOCH$_2$C**H**$_3$). ^{13}C NMR (100 MHz, DMSO-d_6): 169.3 (**C**OOEt); 154.7 (C-2); 139.9 (C-4); 118.3 (C-3); 136.8, 134.0, 130.9, 130.0, 126.2, 122.4, 121.0, 119.1, 116.0, 114.1, 109.7, 104.9 (12 arom. C); 59.7 (COO**C**H$_2$CH$_3$); 23.1 (CH$_3$); 16.1 (COOCH$_2$**C**H$_3$). MS (EI, 70 eV), *m/z* (rel.%): 321 (100) [M$^+$]; 276 (45); 262 (97); 248 (32); 244 (27); 217 (41); 196 (23).

Ethyl 8-chloro-2-oxo-2,11-dihydropyrano[2,3-a]carbazole-3-carboxylate (**7d**): Yellow amorphous powder, m.p. 256–258 °C. Yield 50%. For $C_{18}H_{12}ClNO_4$ (341.8) calculated: 63.26% C, 3.54% H, 4.10% N; found: 63.38% C, 3.50% H, 4.03% N. IR: 3270, 2925, 1729, 1654, 1306. ^{1}H NMR (400 MHz, DMSO-d_6): 12.26 b s, 1 H (H-11, deuterium-exchangeable); 8.87 s, 1 H (H-4); 8.18 s, 1 H (H-7); 7.95–7.90 d, 1 H, *J*(6,5) = 8.2 (H-6); 7.50–7.45 m, 3 H (H-5, H-9, H-10); 4.32–4.26 q, 2 H, *J* = 7.1 (COOC**H**$_2$CH$_3$); 1.36–1.29 t, 3 H, *J* = 7.1 (COOCH$_2$C**H**$_3$). ^{13}C NMR (100 MHz, DMSO-d_6): 168.8 (**C**OOEt); 155.9 (C-2); 140.6 (C-4); 116.7 (C-3); 139.5, 137.9, 132.1, 129.4, 126.1, 121.8, 120.1, 118.7, 115.7, 113.6, 111.6, 109.8 (12 arom. C); 59.7 (COO**C**H$_2$CH$_3$); 14.9 (COOCH$_2$**C**H$_3$). MS (EI, 70 eV), *m/z* (rel.%): 341 (100) [M$^+$]; 343 (28); 296 (47); 282 (95); 268 (32); 237 (39).

Ethyl 2-oxo-2,11-dihydropyrano[2,3-a]carbazole-3-carboxylate (**7e**): Yellow amorphous powder, m.p. 222–224 °C. Yield 68%. For $C_{18}H_{13}NO_4$ (307.3) calculated: 70.35% C, 4.26% H, 4.56% N; found: 70.21% C, 4.30% H, 4.60% N. IR: 3352, 2924, 1746, 1636, 1249. ^{1}H NMR (400 MHz, DMSO-d_6): 12.34 b s, 1 H (H-11, deuterium-exchangeable); 8.94 s, 1 H (H-4); 8.27–8.22 d, 1 H, *J*(6,5) = 8.3 (H-6); 8.17–8.12 d, 1 H, *J*(5,6) = 8.3 (H-5); 7.65–7.61 d, 1 H, *J*(10,9) = 8.2 (H-10); 7.60–7.47 m, 3 H (H-7, H-8, H-9); 4.36–4.27 q, 2 H, *J* = 7.1 (COOC**H**$_2$CH$_3$); 1.36–1.30 t, 3 H, *J* = 7.1 (COOCH$_2$C**H**$_3$). ^{13}C NMR (100 MHz, DMSO-d_6): 171.0 (**C**OOEt); 154.1 (C-2); 138.4 (C-4); 116.3 (C-3); 137.9, 135.1, 134.4, 130.3, 127.8, 124.5, 121.3, 119.3, 116.3, 110.6, 107.4, 106.7 (12 arom. C); 59.1 (COO**C**H$_2$CH$_3$); 16.4 (COOCH$_2$**C**H$_3$). MS (EI, 70 eV), *m/z* (rel.%): 307 (100) [M$^+$]; 262 (40); 248 (94); 215 (16); 182 (12).

The authors are grateful to prof. J. S. Yadav, the Director, ISO quality assurance cell, IICT, Hyderabad and prof. K. V. Ramanathan, the Chairman, NMR research centre, IISc, Bangalore for providing mass spectral data and NMR spectra, respectively.

REFERENCES

1. Knolker H. J., Reddy K. R.: *Chem. Rev.* **2002**, *102*, 4303.
2. Haider N., Sotelo E.: *Chem. Pharm. Bull.* **2002**, *50*, 1479.
3. Long B. H., Rose W. C., Vyas D. M., Matson J. A., Forenza S.: *Curr. Med. Chem., Anticancer Agents* **2002**, *2*, 255.
4. Guillonneau C., Pierre A., Charton Y., Guilbaud N., Berthier L. K., Leonce S., Michel A., Bisagni E., Atassi G.: *J. Med. Chem.* **1999**, *42*, 2191.
5. Hirata K., Ito C., Furukawa H., Itoigawa M., Cosentino L. M., Lee K. H.: *Bioorg. Med. Chem. Lett.* **1999**, *9*, 119.
6. Wang J., Zheng Y., Efferth T., Wang R., Shen Y., Hao X.: *Phytochemistry* **2005**, *66*, 697.
7. Vandana, Rajendra Prasad K. J.: *J. Chem. Res.* **2004**, 717.
8. Danish I. A., Rajendra Prasad K. J.: *Collect. Czech. Chem. Commun.* **2005**, *70*, 223.
9. Knolker H.-J., Wolpert M.: *Tetrahedron* **2003**, *59*, 5317.
10. Hagiwara H., Choshi T., Fujimoto H., Sugino E., Hibino S.: *Tetrahedron* **2000**, *56*, 5807.
11. Danish I. A.: *Ph.D. Thesis*. Bharathiar University, Coimbatore 2004.
12. a) Joseph D., Martarello L., Kirsch G.: *J. Chem. Res., Synop.* **1995**, 350; b) Joseph D., Martarello L., Kirsch G.: *J. Chem. Res., Miniprint* **1995**, 2001.
13. Shanmugansundaram K., Rajendra Prasad K. J.: *Heterocycles* **1999**, *51*, 2163.
14. Sangeetha V., Rajendra Prasad K. J.: *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.* **2006**, *45*, 1951.
15. Furniss B. S., Hannaford A. J., Smith P. W. G., Tatchell A. R.: *Vogel's Text Book of Practical Organic Chemistry*, p. 1052. ELBS with Longman Singapore Publishers Private Ltd., Singapore 1989.
16. Kirsch G. H.: *Curr. Org. Chem.* **2001**, *5*, 507.
17. Gunaseelan A. T., Thiruvalluvar A., Martin A. E., Rajendra Prasad K. J., Butcher R. J.: *Acta Crystallogr., Sect. E* **2007**, *63*, o2410.