

A Facile Synthesis of Quino[2,3-*a*]carbazoles

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Z. Naturforsch. **54b**, 1618–1620 (1999);
received June 14, 1999

1-Oxo-1,2,3,4-tetrahydrocarbazole, *o*-Aminoacetophenone Condensation, Cyclisation, Aerial Oxidation

Condensation of 1-oxo-1,2,3,4-tetrahydrocarbazoles **1a-e** and *o*-aminoacetophenone **2** under acid catalysis afforded a new class of quino[2,3-*a*]carbazoles **3a-e** in good yields. A plausible mechanism for the product formation is also proposed.

In general pyrano, pyrazino and simple benzocarbazole derivatives were reported to have pharmacological properties like antihistaminic, anti-inflammatory, antibiotic and antimicrobial activity [1–11]. Pyridocarbazoles are well known anticancer agents [12–15]. To our knowledge there is no report on the synthesis of quino[2,3-*a*]carbazoles, which can be considered as substituted pyridocarbazoles, probably due to the nonavailability of viable general methods for the construction of this system. The present investigation was aimed to devise a new synthetic route for the hitherto unknown title compounds which can be expected to exhibit anticancer properties. In this connection 1-oxo-1,2,3,4-tetrahydrocarbazole which has a $-\text{CH}_2\text{CO}-$ group is condensed with the amino group of *o*-amino-

acetophenone under acidic conditions as in the Friedländer synthesis of simple quinolines [16–17].

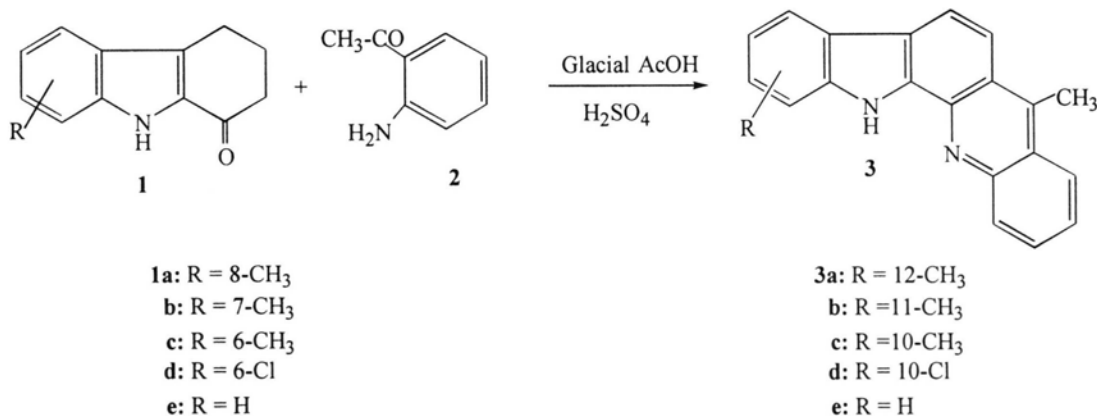
8-Methyl 1-oxo-1,2,3,4-tetrahydrocarbazole (**1a**) prepared according to our reported procedure [6,11] on condensation with *o*-aminoacetophenone **2** in glacial acetic acid in the presence of a drop of concentrated sulphuric acid gave, after work-up, a single product. It showed IR absorptions at 3284 cm^{-1} and 1685 cm^{-1} corresponding to $-\text{NH}$ stretching and $-\text{C}=\text{N}$ vibrations. The ^1H NMR spectrum showed two three proton singlets at δ 2.25 and 2.79 ppm and nine aromatic protons and a NH proton appeared as a multiplet in the 7.22–8.66 region. Elemental analysis and the molecular ion peak at m/e 296 agreed well with the molecular formula $\text{C}_{21}\text{H}_{16}\text{N}_2$. The peaks at m/e 130 and 142 are characteristic of substituted quinoline nucleus and peaks at m/e 115, 130 and 157 confirm the presence of carbazole nucleus. Based on the above mentioned spectral data the product was attested to be 6,12-dimethylquino[2,3-*a*]carbazole (**3a**).

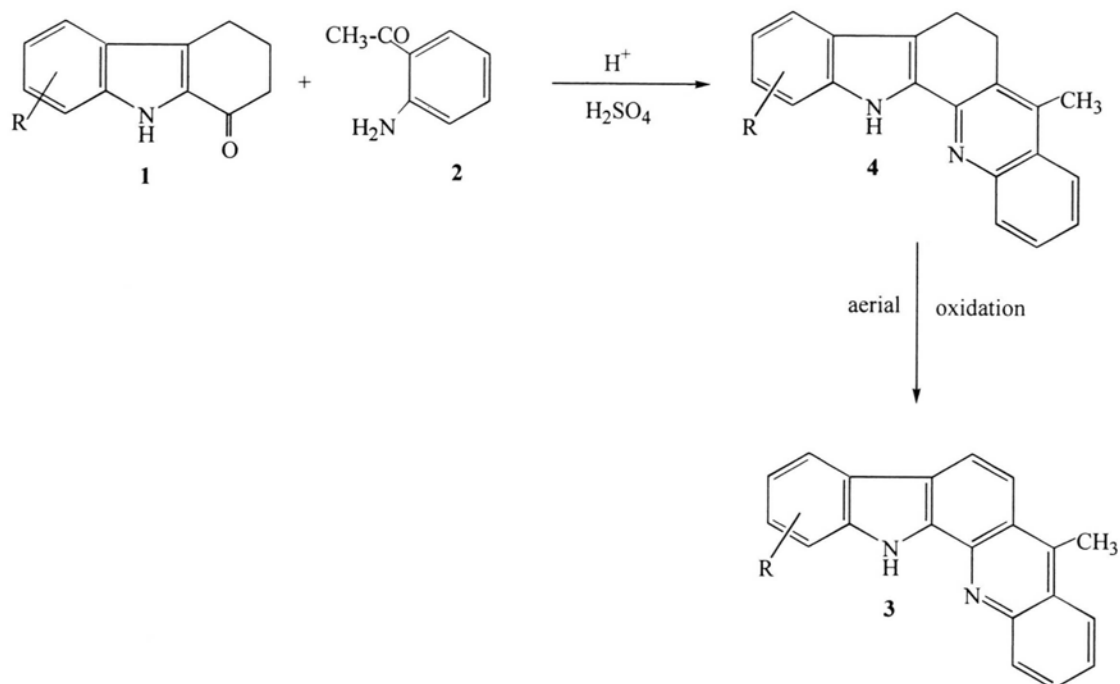
A similar series of compounds **3b**, **3c**, **3d** and **3e** were obtained from **1b**, **1c**, **1d** and **1e** respectively (Scheme 1). A plausible mechanism for the formation of the product **3** comprises a two fold condensation reaction between **1** and **2** followed by an aerial oxidation of the pentacyclic intermediate **4** (Scheme 2).

Experimental

General procedure for the synthesis of quino[2,3-*a*]carbazoles (**3**)

A solution of 1-oxo-1,2,3,4-tetrahydrocarbazole (0.001 mol), *o*-aminoacetophenone (0.001 mol) in



Table I. Physical and spectral data of new quino[2,3-*a*]carbazole derivatives (**3**).

Compound	m.p. (°C) ^a (solvent)	Yield (%)	IR ^b (ν cm ⁻¹)	MS (70 eV) ^c (<i>m/e</i>) (M ⁺)	Molecular formula	Analysis (%) ^d		¹ H NMR ^e
						Calcd	Found	
3a	85 (PE-EA)	68	3284 (-NH) 1685 (-C=N)	296	C ₂₁ H ₁₆ N ₂	C 85.10 H 5.43 N 9.45	84.97 5.31 9.38	2.25 (s, 3H, 12-CH ₃), 2.79 (s, 3H, 6-CH ₃) 7.22–8.66 (m, 10H, 9H-aryl and a NH)
3b	95 (PE-EA)	66	3278 (-NH) 1685 (-C=N)	296	C ₂₁ H ₁₆ N ₂	C 85.10 H 5.43 N 9.45	84.90 5.34 9.31	2.22 (s, 3H, 11-CH ₃), 2.77 (s, 3H, 6-CH ₃) 7.18–8.70 (m, 10H, 9H-aryl and a NH)
3c	165 (PE-EA)	66	3276 (-NH) 1637 (-C=N)	296	C ₂₁ H ₁₆ N ₂	C 85.10 H 5.43 N 9.45	84.95 5.37 9.33	2.23 (s, 3H, 10-CH ₃), 2.77 (s, 3H, 6-CH ₃) 7.36–8.69 (m, 10H, 9H-aryl and a NH)
3d	67 (PE-EA)	64	3222 (-NH) 1654 (-C=N)	316	C ₂₀ H ₁₃ N ₂ Cl	C 75.83 H 4.13 N 8.84	75.71 3.91 8.69	2.65 (s, 3H, 6-CH ₃), 7.12–8.73 (m, 10H, 9H-aryl and a NH)
3e	121 (PE-EA)	62	3284 (-NH) 1637 (-C=N)	282	C ₂₀ H ₁₄ N ₂	C 85.08 H 4.99 N 9.92	84.89 4.90 9.87	2.67 (s, 3H, 6-CH ₃), 7.17–7.90 (m, 11H, 10H-aryl and a NH)

PE Petroleum ether 60–80 °C. EA: Ethyl acetate;

^a uncorrected, measured using Mettler FP5 apparatus and a Boetius microheating table;

^b recorded on a Shimadzu FTIR-8000 Infrared Spectrophotometer;

^c recorded on a Jeol-JMS-D 300 Mass Spectrometer;

^d satisfactory microanalyses were obtained on Carlo Erba 1106 and Perkin-Elmer Model 240 CHN analyzer;

^e NMR spectra were recorded on Varian AMX400 FT-NMR spectrometer using tetramethylsilane as internal reference in CDCl₃;

The chemical shifts are quoted in parts per million (PPM).

glacial acetic acid (10 ml) was refluxed for 8 h in the presence of a drop of concentrated sulphuric acid. The reaction mixture was then cooled and poured into ice water with stirring, extracted with chloroform. The organic layer was dried over anhydrous sodium sulphate and the excess solvent was removed by distillation to yield the crude product. This was purified by column chromatography over silica gel and eluted with petroleum ether – ethyl acetate mixture (95:5).

Experimental data of the quino[2,3-*a*]carbazoles **3a-e** thus produced are collected in Table I.

Acknowledgements

R. B.M thanks Bharathiar University, Coimbatore, for the award of University Fellowship. We acknowledge SIF, IISc, Bangalore and RSIC, CDRI, Lucknow for providing spectral and analytical data.

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