Research Article

Spectral Analysis and Crystal Structures of 4-(4-Methylphenyl)-6-Phenyl-2,3,3a,4-Tetrahydro-1H-Pyrido[3,2,1-jk]Carbazole and 4-(4-Methoxyphenyl)-6-Phenyl-2,3,3a,4-Tetrahydro-1H-Pyrido[3,2,1-jk]Carbazole

J. Kalyana Sundar,1 S. Natarajan,1 S. Chitra,2 Nidhin Paul,3 P. Manisankar,2 S. Muthusubramanian,3 and J. Suresh4

1 School of Physics, Madurai Kamaraj University, Madurai 625 021, India
2 Department of Industrial Chemistry, School of Chemistry, Alagappa University, Karaikudi 630 003, India
3 Department of Organic Chemistry, School of Chemistry, Madurai Kamaraj University, Madurai 625 021, India
4 Department of Physics, The Madura College, Madurai 625 011, India

Correspondence should be addressed to S. Natarajan, s.natarajan50@yahoo.com

Received 13 January 2011; Accepted 13 February 2011

Academic Editors: S. Bellemin-Laponnaz, C. W. Lehmann, and J. C. Menéndez

Copyright © 2011 J. Kalyana Sundar et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

The crystal structures of 4-(4-methylphenyl)-6-phenyl-2,3,3a,4-tetrahydro-1H-pyrido[3,2,1-jk]carbazole (IIa) and 4-(4-methoxyphenyl)-6-phenyl-2,3,3a,4-tetrahydro-1H-pyrido[3,2,1-jk]carbazole (IIb) were elucidated by single crystal X-ray diffraction. Compound (IIa), C28H25N, crystallizes in the triclinic system, space group P-1, with \(a = 8.936(2)\,\text{Å}, b = 10.490(1)\,\text{Å}, c = 11.801(1)\,\text{Å}, \alpha = 102.69(5)^\circ, \beta = 103.27(3)^\circ, \gamma = 93.80(1)^\circ\), and \(Z = 2\). The compound (IIb), C28H25NO, crystallizes in the monoclinic system, space group P2_1/a, with \(a = 11.376(5)\,\text{Å}, b = 14.139(3)\,\text{Å}, c = 13.237(4)\,\text{Å}, \beta = 97.41(3)^\circ\), and \(Z = 4\). In both the structures, the pyrido ring adopts a twist boat conformation and the carbazole molecule has the twisted envelope structure with C3 and C13 at the flap. No classical hydrogen bonds are observed in the crystal structures. Details of the preparation, structures, and spectroscopic properties of the new compounds are discussed.

1. Introduction

Many natural products with carbazole moiety are found to have antitumor properties [1]. The Schiff bases derived from 9-aminocarbazole showed notable activity as agrochemical fungicides [2]. Indolo [2,3-a] carbazole-based inhibitors were synthesized, and they displayed moderate inhibitory activities toward Bacillus anthracis and Mycobacterium tuberculosis, indicating that indolo [2,3-a] carbazoles could serve as promising leads in the development of new drugs to combat anthrax and tuberculosis infections [3]. Natural and synthetic carbazoles, either in a pure substituted or in an annellated substituted form, represent an important and heterogeneous class of anticancer agents. Many carbazole derivatives were tested for cytotoxic activity; some of them have entered clinical trials [4]. A series of N-alkylated 3,6-dihalogenocarbazoles exhibit fungicidal activity against C. albicans and the emerging pathogen Candida glabrata [5]. Although the carbazole motif has been characterized structurally over 700 times, tetrahydrocarbazoles are much rarer, and of the tetracyclic nature, including the pyrido ring, there are actually only six, with the closest being 5,6-Dihydro-8-methyl-4H-pyrazino (3,2,1-jk) carbazole [6]. This paper reports the preparation of two carbazole derivatives and their structural investigations.

2. Experimental

For the preparation of the compound (IIa), a mixture of 2-(3-oxo-1-(4-methylphenyl)-3-phenylpropyl)cyclohexanone
(3 mmol) and phenylhydrazine hydrochloride (6 mmol) in ethanol (20 mL) was stirred for 2 hrs. After the completion of the reaction, the mixture was poured into excess water and the precipitate was filtered off and recrystallized from ethanol (Yield 0.71 g, 72%; m.p. 454 K). For the preparation of compound (IIB), a mixture of 2-(1-(4-methylphenyl)-3-oxo-3-phenylpropyl) cyclohexanone (3 mmol) and phenylhydrazine hydrochloride (6 mmol) in ethanol (20 mL) was stirred for 2 hrs. After the completion of the reaction, the mixture was poured into excess water and the precipitate was filtered off and recrystallized from ethanol [7] (Yield 0.78 g, 66%; m.p. 475 K).

2.1. Structure Determination and Refinement. Single crystal X-ray intensity data for compound (IIa) and (IIB) were collected using a Nonius CAD-4 MACH 3 diffractometer with MoKα (0.71073 Å) radiation at room temperature (293 K). The data reduction was performed with XCAD4 [2, 8]. An absorption correction was made using the ψ-scan method [9]. The structures of both compounds were solved by direct methods using SHELXS97 [10], and all the nonhydrogen atoms were refined anisotropically by full-matrix least-squares on $F^2$ taking all the unique reflections using SHELXL97 [11]. The hydrogen atoms were placed in their calculated positions and included in the refinement using the riding model with C–H $0.93$ Å (–CH) or $0.97$ Å (–CH$_3$) with $U_{eq}$(H) = $1.2U_{eq}$(parent C atom). The crystal data, experimental conditions, and structure refinement parameters for the compounds (IIa) and (IIB) are presented in Tables 1 and 2. Some important bond lengths and bond angles are given in Tables 3 and 4. The molecular structures of compound (IIa) and (IIB) showing the atom numbering scheme using ORTEP 3 [12] are given in Figures 1 and 2, respectively.

### 3. Results and Discussion

#### 3.1. Synthesis of the Compounds. The title compounds, 4-(4-methylphenyl)-6-phenyl-2,3,3a,4-tetrahydro-1H-pyrido[3,2,1-ff]carbazoles, have been prepared from linebreak the diketones, 2-(3-oxo-1-(4-methylphenyl/methoxynonyl)-3-phenylpropyl) cyclohexanones following the
Table 3: Some important bond lengths (Å) and bond angles (°) for compound (IIa).

| Bond                  | Length (Å) | Angle (°) |
|-----------------------|------------|-----------|
| N(7)-C(11C)           | 1.396(3)   |           |
| N(7)-C(7A)            | 1.401(3)   |           |
| N(7)-C(6)             | 1.420(3)   |           |
| C(11C)-C(11B)         | 1.350(3)   |           |
| C(11C)-C(3A)          | 1.485(3)   |           |
| C(11B)-C(11A)         | 1.430(4)   |           |
| C(11B)-C(1)           | 1.494(4)   |           |
| C(3)-C(2)             | 1.524(4)   |           |
| C(2)-C(1)             | 1.525(4)   |           |
| C(11C)-N(7)-C(7A)     | 107.14(19) |           |
| C(11C)-N(7)-C(6)      | 120.06(19) |           |
| C(11C)-C(11B)-C(11A) | 113.92(19) |           |
| C(11C)-C(3A)          | 121.28(16) |           |
| C(11C)-C(11B)-C(1)    | 117.89(17) |           |
| C(11C)-N(7)-C(7A)     | 107.14(19) |           |

3.2. Spectral Data. In the IR spectrum of (IIa), bands appear at 3051 cm⁻¹ (aromatic C–H stretching), 1567 cm⁻¹ (olefinic C=C stretching), 2844 cm⁻¹, and 2923 cm⁻¹ (aliphatic C–H stretching). The identity of the above compound has been ascertained by NMR spectral data. A detailed analysis of the two-dimensional NMR spectra has helped to assign the hydrogens and carbons of interest in these compounds. The numbering for carbons and hydrogens given here for NMR data and crystal structure is for convenience and not exactly the correct way of numbering according to IUPAC rules. Compound (IIa) has a broad quartet at 1.34 ppm (1H, H-3 axial like), a multiplet between 1.75–1.78 ppm (1H, H-3 equatorial like), a multiplet between 1.80–1.87 ppm (1H, H-2 axial like), a multiplet at 2.07–2.12 ppm (1H, H-2 equatorial like), a strong triplet with further fine coupling at 2.73 ppm (1H, H-1 axial like), and a doublet of doublet at 2.82 ppm (1H, J = 15.6 & 5.8 Hz, H-1 equatorial). The H-3a proton appears as a broadened triplet at 3.06 ppm with coupling constant J = 11.7 Hz, while H-4 proton appears as a doublet of doublet at 3.31 ppm (J = 12.2 & 2.4 Hz). A doublet appears at 5.39 ppm, (J = 2.4 Hz), which is assigned to H-5 proton. The H-8 proton appears as a doublet at 6.33 ppm (J = 8.1 Hz) followed by two triplets centering at 6.85 ppm and 7.02 ppm (J = 7.8 Hz). A multiplet appears between 7.14 to 7.24 ppm accounting for five hydrogens. There are seven CH carbons at 112.6, 116.8, 118.2, 119.6, 121.1, 128.5, and 129.1 ppm. Two CH carbon signals appear at 128.1 ppm (merging together). The quaternary carbons appear at 110.7, 128.9, 134.9, 136.1, 136.3, 136.5, 138.2, and 140.1 ppm. Table 5 reveals the...
Figure 1: The molecular structure of compound (IIa) showing the atom numbering scheme. Displacement ellipsoids are drawn at 50% probability level, using ORTEP 3. Hydrogen atoms are drawn as spheres of arbitrary size.

Figure 2: The molecular structure of compound (IIb) showing the atom numbering scheme. Displacement ellipsoids are drawn at 50% probability level, using ORTEP 3. Hydrogen atoms are drawn as spheres of arbitrary size.
Table 5: Two-dimensional NMR data revealing connectivities of different nuclei in compound (IIa).

| Proton | Chemical shifts (ppm) | C,H-COSY connections | H,H-COSY connections | HMBC connections |
|--------|----------------------|----------------------|----------------------|-----------------|
| H-1\* | 2.73 (brt)           | 21.1 (C-1)           | 1.75–1.78, 2.07–2.12 | 110.7           |
| H-1\** | 2.82(dd, J = 15.6, 5.8 Hz) | 1.75–1.78, 2.07–2.12 | 23.2, 28.3, 110.7, 136.5, 136.1 |
| H-2\* | 1.80–1.87 (m)        | 23.2 (C-2)           | 2.73, 2.82           | 21.1, 110.7     |
| H-2\** | 2.07–2.12 (m)        | 1.34                 | 23.2                 |                 |
| H-3\* | 1.34 (brq)           | 28.3 (C-3)           | 1.75–1.78, 3.04      | 21.1, 39.2, 136.1, 136.5 |
| H-3\** | 1.75–1.78 (m)        | 2.07–2.12            | 21.1, 39.2, 136.1, 136.5 |
| H-3a  | 3.06 (brt)           | 39.2 (C-3a)          | 1.34                 |                 |
| H-4   | 3.31(dd, J = 12.2, 2.4 Hz) | 46.6 (C-4)          | 3.04                 | 28.3, 39.2, 116.8, 128.1, 128.9, 138.2 |
| H-5   | 5.39(d, J = 2.4 Hz)  | 116.9 (C-5)          | 3.31                 | 39.2, 46.6, 134.9, 138.2, 140.1 |
| H-8   | 6.33(d, J = 8.1 Hz)  | 112.6 (C-8)          | 6.85                 | 119.6, 128.9    |
| H-9   | 6.85(t, J = 7.8 Hz)  | 121.1 (C-9)          | 6.33                 | 116.1, 134.9    |
| H-10  | 7.02(t, J = 7.8 Hz)  | 119.6 (C-10)         | 6.85                 | 112.6, 128.9    |
| H-11  | 7.40–7.50 (m)\***   | 128.3                | 7.02                 | 21.1, 110.7, 121.1, 128.9, 135.0 |

\* Axial like  \
\** Equatorial like  \
\*** Appears along with other aromatic hydrogens.

Table 6: Two-dimensional NMR data revealing connectivities of different nuclei in compound (IIb).

| Proton | Chemical shifts (ppm) | C,H-COSY connections | H,H-COSY connections | HMBC connections |
|--------|----------------------|----------------------|----------------------|-----------------|
| H-1\* | 2.73 (brt)           | 20.8 (C-1)           | 1.81–1.88, 2.08–2.13 | 110.7           |
| H-1\** | 2.83(dd, J = 15.6, 5.6 Hz) | 1.81–1.88, 2.08–2.13 | 23.2, 28.3, 110.7, 136.1, 136.5 |
| H-2\* | 1.81–1.88 (m)        | 23.2 (C-2)           | 2.73, 2.83           | 21.1, 39.2, 136.5 |
| H-2\** | 2.08–2.13 (m)        | 1.35                 | 23.2                 |                 |
| H-3\* | 1.35 (brq)           | 28.3 (C-3)           | 1.81–1.88, 3.06      | 21.1, 39.2, 136.5 |
| H-3\** | 1.76–1.78 (m)        | 2.08–2.13            | 21.1, 39.2, 136.5    |
| H-3a  | 3.06 (brt)           | 39.3 (C-3a)          | 1.35                 | 46.2            |
| H-4   | 3.32(dd, J = 12.0, 2.4 Hz) | 46.2 (C-4)          | 3.06                 | 28.3, 39.2, 116.9, 128.1, 128.9, 138.2 |
| H-5   | 5.39(d, J = 2.4 Hz)  | 116.9 (C-5)          | 3.32                 | 39.3, 46.2, 134.9, 138.2, 140.1 |
| H-8   | 6.33(d, J = 8.4 Hz)  | 112.6 (C-8)          | 6.85                 | 119.6, 128.9    |
| H-9   | 6.85(t, J = 7.8 Hz)  | 121.1 (C-9)          | 7.02                 |                 |
| H-10  | 7.02(t, J = 7.8 Hz)  | 119.6 (C-10)         | 7.40–7.50            | 112.6, 128.9    |
| H-11  | 7.40–7.50 (m)\***   | 128.3                | 7.02                 | 110.7, 121.1, 128.9, 135.0 |

\* Axial like  \
\** Equatorial like  \
\*** Appears along with other aromatic hydrogens.

Figure 3: Preparation of II.
homonuclear and heteronuclear connectivities of different nuclei in this compound. Assignment of different carbons and hydrogens for compound (IIa) based on the connectivity studies is shown in Figure 4.

It is clear that the phenyl substituent at the olefinic carbon goes out of plane to the rest of the ring. This ultimately leads to the shielding of the peri hydrogen and also the other olefinic hydrogen, with the ring current effect being responsible for this shielding. The crystal structure also confirms this; the phenyl ring is twisted by nearly 38º. The olefinic hydrogen (5.39 ppm) and the benzylic hydrogen (3.31 ppm) have poor coupling between them indicating that they may probably be nearly orthogonal to each other. This is confirmed in the crystal structure. The considerable coupling of 12.0 Hz between the benzylic hydrogen and the ring junction hydrogen (3.06 ppm) amounts to that they are antiparallel to each other. This is again found to be corroborated in the solid state, with the torsion angle between these hydrogens being 177.6º. This ring junction hydrogen has a broad triplet with coupling nearly 11.7 Hz suggesting that it assumes an axial-like arrangement with another axial coupling with the ring vicinal hydrogen. The inspection of the crystal structure suggests this could be the axial hydrogen vicinal to the ring junction hydrogen which also experiences the anisotropic shielding of the p-methylphenyl ring.

The NMR data for compound (IIb) are very similar to that of compound (IIa), and Table 6 summarizes the connectivity observed in the two-dimensional NMR spectra of (IIb), and Figure 5 indicates the assignment of different
carbons and hydrogens of (IIb). The significant IR bands observed for (IIb) are 1428, 1450, 1504, 1567, 1619, 2922, 2835, 3016, and 3043 cm$^{-1}$.

3.3. Crystal Structure. The pyrido ring of both the compounds adopts a twist boat conformation. The carbazole molecule of compounds (IIa) and (IIb) has the twisted envelope structure with atoms C3 and C13 at the flap, respectively, and they have the distance of 0.777(3) Å and 0.651(2) Å from the mean plane of the carbazole. The most favoured orientation of the phenyl and methylphenyl/methoxyphenyl rings in the structure is that their least-square mean planes are inclined toward the opposite directions with respect to least-square mean plane of the carbazole rings and they are essentially planar and perpendicular to each other by the planar angles, 80.72(3)$^\circ$ and 82.33(3)$^\circ$, in compounds (IIa) and (IIb), respectively. In the crystal structure of (IIa), H3A and H4 have the transconformation with the torsion angle of 176.60(2)$^\circ$. In compound (IIb) too, similar conformation is found. The structures are stabilized by weak intermolecular interactions. Further, no classical hydrogen bonds are observed in the crystal structure. From the crystal structures, it is seen that there is no change in the ideal nature of the moiety due to the substitution of methylphenyl or methoxyphenyl groups.

Acknowledgments

One of the authors (J. Kalyana Sundar) thanks the UGC for the RFSMS fellowship. S. Natarajan thanks the CSIR for the funding provided under the Emeritus Scientist Scheme. Crystallographic data (excluding structure factors) for the structures of (IIa) and (IIb) reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication no. CCDC: 791730 and 796130. Copies of the data can be obtained, free of charge, on application to, CCDC, 12 Union Road, Cambridge, CB2 1 EZ UK; Fax: 044-1223-336033; Email: deposit@ccdc.cam.uk or at: http://www.ccdc.cam.ac.uk/.

References

[1] C. Zhang, C. Albermann, X. Fu et al., “RebG- and RebM-catalyzed indolocarbazole diversification,” ChemBioChem, vol. 7, no. 5, pp. 795–804, 2006.
[2] Z. H. Li, J. F. Li, and Y. Gang, “Synthesis and Biological Activity of Carbazole Schiff Bases,” Yingyong Huaxue, vol. 24, no. 9, p. 1074, 2007.
[3] S. Guo, S. K. Tipparaju, S. D. Pegan et al., “Natural product leads for drug discovery: isolation, synthesis and biological evaluation of 6-cyano-5-methoxyindolo[2,3-a]carbazole based ligands as antibacterial agents,” Bioorganic and Medicinal Chemistry, vol. 17, no. 20, pp. 7126–7130, 2009.
[4] C. Asche and M. Demeunynck, "Antitumor carbazoles," Anti-Cancer Agents in Medicinal Chemistry, vol. 7, no. 2, pp. 247–267, 2007.
[5] K. Thevissen, A. Marchand, P. Chaltin, E. M. K. Meert, and B. P. A. Cammue, “Antifungal carbazoles,” Current Medicinal Chemistry, vol. 16, no. 17, pp. 2205–2211, 2009.