

# Nuclear Magnetic Resonance VI[1]. Some Quantitative Applications of Carbon-13 NMR Spectroscopy to Phenylindoles

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**Summary.** The number of carbons represented by each signal of the phenylindoles **1**, **4**, and **5** is measured quantitatively by integration of their <sup>13</sup>C NMR spectra, recorded after adding chromium(III) acetylacetonate to the sample solutions as a paramagnetic relaxation agent. Their carbon chemical shifts are assigned unambiguously; the literature assignments of **4** are confirmed. By a comparative study of the carbon chemical shifts of **1**, **4**, and **5**, those of **2** and **3** are also assigned. The *ortho* carbons of the phenyl group of **4** resonate upfield with respect to the *para* carbon. The *ortho* carbons of the 2- and 3-phenyl moieties of **1–3** and **5**, however, are found to absorb downfield from the corresponding *para* carbons, probably because of steric and/or electronic effects exerted by their neighbouring phenyl group.

**Keywords.** Phenylindoles; Quantitative <sup>13</sup>C NMR; Chromium(III) acetylacetonate.

## Kernresonanzspektroskopie, 6. Mitt. [1]. Einige quantitative Anwendungen der <sup>13</sup>C-NMR-Spektroskopie auf Phenylindole

**Zusammenfassung.** Die Anzahl der durch jedes Signal der Phenylindole **1**, **4** und **5** repräsentierten Kohlenstoffatome wird durch Integration der nach Zusatz von Chrom(III)acetylacetonat als Relaxationsreagens aufgenommenen <sup>13</sup>C-NMR-Spektren bestimmt. Ihre chemischen Verschiebungen werden eindeutig zugeordnet; die Literaturwerte für **4** werden bestätigt. Durch eine vergleichende Untersuchung der <sup>13</sup>C-chemischen Verschiebungen von **1**, **4** und **5** können jene von **2** und **3** ebenfalls zugeordnet werden. Die *ortho*-Kohlenstoffe der Phenylgruppe von **4** sind gegenüber den *para*-Kohlenstoffatomen zu höherem Feld verschoben. Für die 2- und 3-Phenyl-Substituenten von **1–3** und **5** kehren sich die Verhältnisse um, wahrscheinlich wegen sterischer und/oder elektronischer Effekte der benachbarten Phenylgruppe.

## Introduction

Interest in the study of <sup>13</sup>C NMR spectra of indoles has been shown by a number of workers [2–11]. Gilchrist *et al.* [6] observed that the *para* carbons of the phenyl

groups of 1-, 2-, and 3-phenylindoles resonate downfield ( $\Delta\delta = 1.5\text{--}2.0$  ppm) from their *ortho* carbons in their  $^{13}\text{C}$  NMR spectra. We however, noticed recently that the *para* carbons of the phenyl groups of a number of indoles [12, 13], *N*-methylindoles [12, 13], and acylindoles [14, 15] resonate upfield ( $\Delta\delta \cong 0.06\text{--}2.72$  ppm) from the corresponding *ortho* carbons. We also observed recently, on the other hand, that the *para* carbons of some of the phenyl groups of *N*-formylindoles [16] resonate downfield ( $\Delta\delta \cong 0.11\text{--}0.31$  ppm) from their *ortho* carbons, whereas the *ortho* and the corresponding *para* carbons of the phenyl groups of a number of *N*-acetylindoles [1, 14] possess the same chemical shift.

We obtained 1-ethyl-2,3-diphenylindole (**1**) and 1-benzyl-2,3-diphenylindole (**2**) by reducing the corresponding 1-acylindoles with diborane [17] and prepared **3** for other purposes [14, 18–20]. We have measured their  $^{13}\text{C}$  NMR spectra, as these do not seem to have appeared in the literature so far. The number of carbons represented by each  $^{13}\text{C}$  NMR signal of some phenylindoles was evaluated earlier by us only qualitatively on the basis of their relative intensities [1, 12–16]. Since this method is not always reliable in  $^{13}\text{C}$  NMR spectroscopy, we considered it worthwhile to determine accurately the number of carbons represented by each  $^{13}\text{C}$  NMR signal of some model phenylindoles by integration and thereby to verify our present assignments of the chemical shifts to all the carbons of **1–3** and our earlier assignments of other phenylindoles [1, 12–16]. We also intended to throw some light on the observations of *Gilchrist et al.* [6] *vis-a-vis* our own [1, 12–16], regarding the chemical shift assignments of the *ortho* and *para* carbon atoms of these phenylindoles. We selected **1**, **4**, and **5** as our model compounds for this purpose.

## Results and Discussion

*Shoolery* [21] showed that all the carbons in a compound can be determined accurately by integration of its  $^{13}\text{C}$  NMR spectrum by adding a paramagnetizing

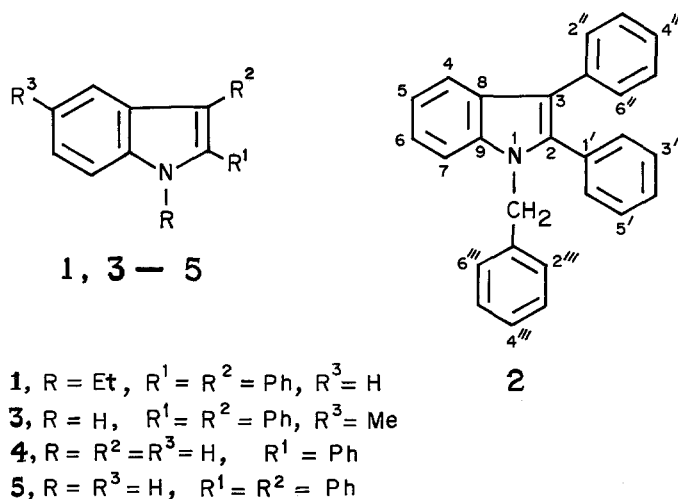


Fig. 1.

relaxation agent to the solution of the sample which provides a relaxation mechanism by which the enhancement of the Nuclear *Overhauser* Effect (NOE) due to dipole–dipole relaxation can leak away as it is generated. Therefore, the difference in NOE factors of different types of carbons of the sample molecule approaches zero. We utilized this technique by using chromium(III) acetylacetonate (Cr(*acac*)<sub>3</sub>) and quantitatively determined the number of carbons represented by each <sup>13</sup>C NMR signal of our model compounds **1**, **4**, and **5** by integration of their spectra. For a comparative study of the results, we have also measured the <sup>13</sup>C NMR spectra of **1–3** without relaxation reagent. Our results are presented herein.

The <sup>13</sup>C NMR chemical shift assignments of **1–3**, **4**, and **5** are presented in Table 1 along with the literature chemical shifts of the carbons of **4** [6] and **5** [7] for comparison. The observed intensity of each <sup>13</sup>C NMR signal of **1**, **4**, and **5** with

**Table 1.** <sup>13</sup>C NMR chemical shift assignments<sup>a</sup> of **1–3**, **4**, and **5**

	<b>1</b> <sup>b,d</sup>	<b>1</b> <sup>c,e</sup>	<b>2</b> <sup>f</sup>	<b>3</b> <sup>g</sup>	<b>4</b> <sup>b,c,h</sup>	<b>5</b> <sup>b,c,h</sup>
C-2	136.93 (45)	137.17 (29)	137.81	135.16	137.87 (32)	135.66 (11)
					137.4	135.7
C-3	115.17 (48)	115.39 (28)	115.72	114.56	98.96 (33)	114.71 (8)
					98.5	114.9
C-4	119.49 (32)	119.73 (68)	119.69	124.16	120.35 (52)	119.43 (28)
					119.7	120.3
C-5	121.80 (32)	121.98 (63)	122.32	128.93	121.80 (55)	122.42 (25)
					121.2	122.5
C-6	119.86 (30)	120.04 (61)	120.38	119.10	119.61 (51)	120.21 (27)
					119.1	119.5
C-7	109.53 (32)	109.68 (55)	110.44	110.46	111.54 (52)	110.84 (19)
					110.9	110.8
C-8	127.85 <sup>i</sup>	128.01 <sup>k</sup>	127.43	127.62	129.01 <sup>m</sup>	128.49 (26)
					128.2	
C-9	135.83 <sup>j</sup> (38)	136.08 <sup>l</sup> (44)	137.02	134.12	137.46 (33)	134.91 (10)
					136.8	134.9
C-1'	131.96 (50)	132.26 (39)	131.84	129.55	132.49 (39)	132.33 (13)
					132.0	
C-2', C-6'	127.85 <sup>i</sup>	128.01 <sup>k</sup>	128.29	127.96	125.19 (99)	127.98 (54)
					124.7	
C-3', C-5'	129.52 (80)	129.77 (112)	129.88	128.38	129.01 <sup>m</sup>	128.33 <sup>n</sup>
					128.2	

(Continued)

**Table 1.** (Continued)

	<b>1</b> <sup>b-d</sup>	<b>1</b> <sup>e,e</sup>	<b>2</b> <sup>f</sup>	<b>3</b> <sup>g</sup>	<b>4</b> <sup>b,e,h</sup>	<b>5</b> <sup>b,e,h</sup>
C-4'	125.16 (28)	125.34 (61)	125.54	126.02	127.49 (47) 126.7	126.01 (26)
C-1''	134.97 <sup>j</sup> (37)	135.20 <sup>l</sup> (32)	135.12	132.68		133.89 (12)
C-2'', C-6''	128.14 (77)	128.32 (126)	128.59	128.38		128.33 <sup>n</sup>
C-3'', C-5''	130.74 (73)	131.01 (123)	131.04	130.08		129.93 (61)
C-4''	127.02 (46)	127.30 (42)	128.10	127.40		127.39 (28)
C-1'''			138.09			
C-2''', C-6'''			126.09			
C-3''', C-5'''			128.10			
C-4'''			127.08			

<sup>a</sup>The numbering of the carbons corresponds to that indicated in structure **2**; <sup>b</sup>the spectrum was recorded after adding Cr(acac)<sub>3</sub>, and the signals were integrated; <sup>c</sup>relative intensity of each carbon signal is presented in parentheses in the second vertical row; <sup>d</sup>N-CH<sub>2</sub>-CH<sub>3</sub>: δ = 38.29 (24) and 15.06 ppm (27); <sup>e</sup>N-CH<sub>2</sub>-CH<sub>3</sub>: δ = 38.50 (45) and 15.23 ppm (39); <sup>f</sup>N-CH<sub>2</sub>-.: δ = 47.54 ppm; <sup>g</sup>5-CH<sub>3</sub>: δ = 21.36 ppm; <sup>h</sup>carbon chemical shifts from the literature [6, 7] (as far as available) are quoted in the vertical row for direction comparison; <sup>i</sup>total intensity of the signal at δ = 127.85 ppm for C-8, C-2', and C-6': 90; <sup>j</sup>interchangeable; <sup>k</sup>total intensity of the signal at δ = 128.01 ppm for C-8, C-2', and C-6': 171; <sup>l</sup>interchangeable; <sup>m</sup>total intensity of the signal at δ = 129.01 ppm for C-8, C-3', and C-5': 122; <sup>n</sup>total intensity of the signal at δ = 128.33 ppm for C-3', C-5', C-2'', and C-6'': 120

addition of Cr(acac)<sub>3</sub> and that of every signal of **1** without it are also given for comparison. In this connection, it may be mentioned here that the <sup>13</sup>C NMR chemical shift assignments of **5** are recorded in the literature [7] without those of the carbons of its two phenyl groups.

A comparison of the relative intensities of the <sup>13</sup>C NMR signal of each carbon of **1** measured by integration with and without Cr(acac)<sub>3</sub> shows a wide range of variations. Only those relative intensities which were obtained with addition of Cr(acac)<sub>3</sub> give a quantitative measure. It may be noted that some of the signals of **1**, **4**, and **5**, whose intensities were measured in presence of Cr(acac)<sub>3</sub> represent two to four carbons each. From these observations, the chemical shifts were assigned to all the carbons of **1**, **4**, and **5** unambiguously and the chemical shift assignments to all the carbons of **4** by Gilchrist *et al.* [6] were confirmed. By comparing the chemical shifts of **1**, **4**, and **5** with those of **2** and **3**, those could also be assigned (Table 1). Our assignments are in accordance with those reported in the literature for other indoles [22]. Our assignment of chemical shifts to all carbons of **5** also fits well to those reported in the literature for its indole moiety [7], except for C-4 and C-6. We have suggested a reversal of the literature assignments of the chemical shifts of these two

carbons of **5** (Table 1), purely on the basis of the steric factor, as reported in the cases of 3-phenylindole [6] and other 3-substituted indoles [3, 10, 22, 23]. Our results also support our earlier assignments of chemical shifts to all carbons of a number of phenylindoles [1, 12–16].

It may be noted from Table 1 that the *ortho* carbons of the phenyl group of **4** resonate upfield ( $\Delta\delta = 2.3$  ppm) from its *para* carbon. However, the *ortho* carbons of the 2-phenyl moiety of **1–3** and **5** absorb downfield ( $\Delta\delta \cong 1.94$ – $2.75$  ppm) from the corresponding *para* carbons. Also, the *ortho* carbons of their 3-phenyl substituent resonate downfield ( $\Delta\delta \cong 0.49$ – $1.12$  ppm) from the corresponding *para* carbons. This difference of chemical shifts of the *ortho* and *para* carbons of the phenyl groups of 1-, 2-, and 3-phenylindoles [6] from those of the corresponding carbons of **1–3** and **5** may be due to steric and/or electronic effects of the neighbouring phenyl substituent in the latter indoles.

## Experimental

The <sup>13</sup>C NMR spectra were recorded on a Varian CFT-20 NMR spectrometer operating at 20.0 MHz at ambient temperature ( $\sim 24$  °C). The spectra were run in CDCl<sub>3</sub> for **1–3** and **5** and DMSO-d<sub>6</sub> for **4**, the solvents serving as internal lock and internal standard substances, in tubes having an outer diameter of 8 to 10 mm. All solutions were about 7–15% in concentration. The chemical shifts reported are given in  $\delta$  (ppm) downfield from TMS;  $\delta_{TMS} = \delta_{CDCl_3} + 76.9$  ppm =  $\delta_{DMSO-d_6} + 39.6$  ppm. The spectra were recorded with a sweep width of 4000 Hz 8 k data points; a 12  $\mu$ s pulse (approximately 60° tilt angle) was employed with a delay of approximately 2 s between pulses. For a quantitative estimation of the number of carbons represented by each signal by integration of the spectra of **1**, **4**, and **5**, a 0.1 M solution of Cr(acac)<sub>3</sub> was added to the sample solutions and the spectra were recorded following Shoolery's technique [21] using a 7–8 s delay between the pulses. <sup>13</sup>C assignments were supported by the observation of C-H coupling, but only the completely proton decoupled spectra are reported. The preparation of **1** and **2** is described elsewhere [17], and **3** [24], **4** [25, 26], **5** [26], and Cr(acac)<sub>3</sub> [27] were prepared by published procedures.

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