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Naphthopyrones, Part II[1]
Carbon-13 Magnetic Resonance Spectral Studies of Some Methylnaphthopyran-2-one and Methylnaphthopyran-4-one Derivatives

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Assignments of ^{13}C chemical shifts and $^{13}C-^{1}H$ coupling constants are presented for four methylnaphthopyrone derivatives. Differentiation between the benzocoumarin and benzochromone series is best performed by consideration of the carbonyl chemical shift and coupling pattern.

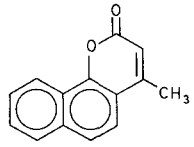
(Keywords: Carbon-13 NMR; Naphthopyrones; Benzocoumarin; Benzochromone)

Naphthopyrone, 2. Mitt.:
^{13}C-NMR einiger Methylnaphthopyran-2-one und Methylnaphthopyran-4-one

Es werden die Zuordnungen der chemischen Verschiebungen der ^{13}C-Resonanzen und der $^{13}C-^{1}H$-Kopplungen für vier Methylnaphthopyrone diskutiert. Die Unterscheidung zwischen der Benzocumarin- und der Benzochromon-Reihe erfolgt am besten mittels chemischer Verschiebungen und dem Kopplungsmuster.

Introduction

During the course of the identification of *Hantzsch* and *Zürchers* "dimethyldicoumarin" the ^{13}C-NMR spectra of the benzocoumarin derivatives 4-methyl-2*H*-naphtho[1,2−*b*]pyran-2-one (**1**) and 1-methyl-3*H*-naphtho[2,1−*b*]pyran-3-one (**2**) were examined[2]. The present paper describes the spectra of these compounds in greater detail, together with the spectra of the benzochromone derivatives 2-methyl-4*H*-naphtho[1,2−*b*]pyran-4-one (**3**) and 3-methyl-1*H*-naphtho-[2,1−*b*]pyran-1-one (**4**).



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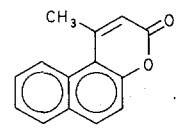

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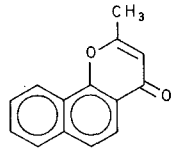

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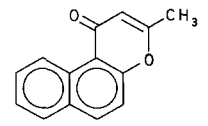

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Carbon-13 NMR spectral studies of coumarin derivatives have attracted considerable interest, and have recently been reviewed[3]. Detailed analyses of the proton coupled spectrum of coumarin have been presented by *Cussans* and *Huckerby*[4] and by *Chang* et al.[5]. However, apart from the earlier brief report from these laboratories[2] no other studies of the benzocoumarin (naphthopyran-2-one) system have appeared, although a partial analysis of the spectrum of the sulphur analogue, 2*H*-naphtho[1,2—*b*]thiopyran-2-thione is available[6].

Investigations of the chromone series are less numerous. The ^{13}C-NMR spectrum of chromone was first reported in 1975 by *Kingsbury* and *Looker*[7], their study also included a number of 2-phenylchromone (flavone) derivatives. Further investigations of the spectrum of chromone have subsequently appeared, the shift assignments are generally in agreement apart from those for the closely separated C-5 and C-6 signals[8—13].

The fully coupled spectrum of chromone and some methyl and phenyl derivatives have been reported by *Huckerby* and *Sunman*[10], the coupled spectrum of 6-acetoxy-4′,7-dimethoxyisoflavone (**5**) has also been presented by *Jha* et al.[14].

Studies of the benzochromone (naphthopyran-4-one) system are very scarce, and as far as the present author is aware the only report to date is that for the linear derivative rubrofusarin dimethyl ether studied by *Leeper* and *Staunton*[15] in the course of their investigation of the biosynthesis of the parent polyketide.

The chemical shifts reported in this paper should provide useful information for the identification of naphthopyrone derivatives.

Results and Discussion

The proton decoupled ^{13}C-NMR spectrum of a methylnaphthopyrone derivative should contain a total of 14 signals, comprising a methyl peak, 7 methine peaks and 6 low intensity quaternary peaks. In the case of **1**, **2** and **3** all 14 peaks were clearly resolved, however, for **4** only 13 peaks were present with two of the quaternary peaks overlapped, as confirmed by the "enhanced quaternary" technique[16]. The ^{13}C chemical shifts are reported in Table 1 and ^{13}C—^{1}H coupling constants in Table 2.

Assignments of the signals were made by comparison with the respective coumarin[4,5] and chromone[10] shieldings where appropriate, and by reference to other suitable model compounds such as 1-naphthol[17], 4-methylphenanthrene[18], 12-methylbenz(a)anthracene[19], phenanthrene-1,4-quinone[20] and benz(a)anthracene-7,12-dione[20]. Assignments were then verified by examination of the proton coupled spectra.

The alkyl signals for **1**, **3** and **4** appeared in the 19–20 δ region, characteristic of an aromatic methyl in an unhindered environment. However, the methyl signal of **3** was shifted downfield to 26.4 δ by a *peri*-proximity effect, a useful diagnostic test which may be used for the identification of this type of *angular* isomer as reported earlier[2]. In the proton coupled spectrum the methyl signals each appeared as a quartet of doublets, the fine splitting being due to long range (^{3}J) coupling to the unsubstituted pyrone ring proton. The magnitudes of the couplings were found to be in accordance with the known relationship[21] with the appropriate ^{1}H—^{1}H *vicinal* coupling constants, *viz*: $J_{CH} = J_{HH} \times 0.6$.

Through the use of $J_{34} = 9.58$ Hz for coumarin[22] and $J_{23} = 6.05$ Hz for chromone[23], calculated values for the methyl splittings for **1** and **2** of 5.8 Hz and for **3** and **4** of 3.6 Hz were obtained, in good agreement with the experimental results (see Table 2). The enhanced splitting (6.7 Hz) experienced for the methyl group of **2**, compared with the normal value found for 4-methylcoumarin (5.5 Hz)[24], must presumably result from the effects of *peri*-substitution.

The assignments and characteristics of the quaternary carbons will now be considered, the carbonyl carbons were assigned first. For **1** and **2** the absorption appeared at ca. 160 δ consistent with the shieldings for coumarin[4,5] and for 2-quinolone[25], whilst for **3** and **4** a downfield shift to ca. 180 δ occurred consistent with chromone[17] and with 4-quinolone[25]. This significant shielding difference for the carbonyl carbon (ester *vs.* ketone type) presents a valuable technique for the distinction between the two series of compounds. A further dissimilarity was also evident in the proton coupled spectrum. The most significant long range couplings for aromatic system result from interactions over three bonds ($^{3}J = 4$–

Table 1. ^{13}C-*NMR chemical shifts* (δ, *ppm*)

	1	2	3	4
C-1	—	154.3	—	180.4
C-2	161.1	116.7	165.6	113.7
C-3	114.5	160.3	112.1	163.5
C-4	153.6	—	178.4	—
C-5	120.5	117.9	121.0	117.7
C-6	124.3	133.8	125.3	135.2
C-7	127.9	129.9	128.4	128.3
C-8	128.8	125.6	129.4	127.3
C-9	127.3	125.2	127.3	129.2
C-10	122.8	128.0	122.5	126.6
C-4a	115.4	154.9	120.1	157.9
C-6a	135.0	131.5	136.1	130.7
C-10a	123.4	130.4	124.2	130.7
C-10b	150.9	114.6	154.2	116.9
CH_3	19.2	26.4	20.5	19.8

Table 2. $^{13}C-^{1}H$ *coupling constants (Hz)*

	1	2	3	4
C=O	J_{23} 4.3	J_{32} 3.7	J_{45} 2.4	—
C—CH_3	J_{45} 3.0	—	J_{23} 6.2	J_{32} 6.2
	$J_{4\cdot CH_3}$ 6.1	$J_{1\cdot CH_3}$ 6.1	$J_{2\cdot CH_3}$ 6.2	$J_{3\cdot CH_3}$ 6.2
CH	J_{33} 169.7	J_{22} 169.7	J_{33} 166.7	J_{22} 166.7
	$J_{3\cdot CH_3}$ 5.5	$J_{2\cdot CH_3}$ 6.2	$J_{3\cdot CH_3}$ 3.7	$J_{2\cdot CH_3}$ 3.7
C-5	J_{55} 161.7	J_{55} 167.2	J_{55} 166.6	J_{55} 166.0
C-6	J_{66} 162.3	J_{66} 163.6	J_{66} 163.0	J_{66} 162.4
	J_{67} 4.9	J_{67} 4.9	J_{67} 4.3	J_{67} 4.9
C-7	J_{77} [a]	J_{77} 161.1	J_{77} 160.5	J_{77} [a]
	J_{76}	J_{76} 4.9	J_{76} 4.9	J_{76}
	J_{79}	J_{79} 6.1	J_{79} 6.7	J_{79}
C-8	J_{88} 161.7	J_{88} 162.4	J_{88} 161.1	J_{88} 166.6
	$J_{8.10}$ 8.6	$J_{8.10}$ 7.9	$J_{8.10}$ 8.5	$J_{8.10}$ [a]
C-9	J_{99} 163.7	J_{99} 160.5	J_{99} 162.0	J_{99} 160.0
	J_{97} 7.9	J_{97} 6.7	J_{97} 7.9	J_{97} 7.3
C-10	$J_{10.10}$ 164.8	$J_{10.10}$ 161.7	$J_{10.10}$ 163.6	$J_{10.10}$ 161.7
	$J_{10.8}$ [b]	$J_{10.8}$ 7.9	$J_{10.8}$ [b]	$J_{10.8}$ 8.5
C-4a	m	m	m	$J_{4a\cdot 6}$ 11.0
				$J_{4a\cdot 5}$ 2.4
C-6a	m	m	m	m
C-10a	m	m	m	m
C-10b	m	m	m	m
CH_3	J_{CH} 128.2	J_{CH} 128.8	J_{CH} 129.3	J_{CH} 129.1
	$J_{CH_3\cdot 3}$ 5.5	$J_{CH_3\cdot 2}$ 6.7	$J_{CH_3\cdot 3}$ 3.0	$J_{CH_3\cdot 2}$ 2.8

[a] Couplings obscured.
[b] Second order spectrum observed, not analysed.

10 Hz) whilst only small couplings occur over two or four bonds[26]. However, with heteroaromatic compounds, quite large two bond couplings can occur with a nucleus which is *ortho* to the heteroatom, *viz* J_{23} and $J_{8a\cdot8}$ in coumarin[5], J_{23} and J_{32} in chromone[10] and J_{23} and J_{32} in quinoline[27]. For the carbonyl carbon of **1** and **2** a ^2J coupling ($J \sim 4$ Hz) was accordingly observed, consistent with the behaviour of coumarin[4,5], whilst for **3** and **4** no such interaction was apparent, since the carbonyl carbon was no longer *ortho* to the oxygen. Previously, *Huckerby* and *Sunman*[10] had only observed multiplets for the carbonyl carbons of the chromone derivatives studied. The different coupling patterns at the carbonyl carbons therefore represents a further technique for the differentiation between benzocoumarin and benzochromone derivatives. The carbonyl carbon of **3** also featured a ^3J (*peri*) coupling ($J_{45} = 2.4$ Hz) consistent with the interactions found[14] for **5** and in naphthoquinone derivatives[28].

The shielding and coupling characteristics of the quaternary carbons bearing the methyl group were dependent upon their proximity to the adjacent ring oxygen. Accordingly, the signals for **3** and **4** appeared downfield of those for **1** and **2** and were also involved in an additional two bond coupling to the pyrone ring proton. All the signals exhibited a quartet splitting to the methyl protons, this coupling is close to 6 Hz and is independent of the position of substitution[10,27].

The assignments of C-4a and of C-10b were generally made next. The latter signal was of extremely low intensity due to the lack of any nearby ring protons which resulted in a particularly long relaxation time. The signal was far downfield in **1** and **3** since it was bonded to oxygen and far upfield in **2** and **4** when it was *ortho* to the oxygen. In the coupled spectrum the peak appeared as a multiplet (frequently obscured by other signals) which has not been analysed. The shieldings of C-4a followed the reverse trends as those for C-10b, again in the coupled spectrum the signal was generally a multiplet, however, a notable exception was the well resolved doublet of doublets obtained for **4**. The splittings have been assigned as $^3J_{4a\cdot6} = 11.0$ Hz and $^2J_{4a\cdot5} = 2.4$ Hz, other protons being very distant. The coupling to H-6 is unexpectedly very large considering that *Huckerby* and *Sunman*[10] gave ca. 9 Hz for the appropriate splitting in 2-methylchromone. The coupling to H-5 is very similar to $^2J_{8a\cdot8}$ in coumarin (2.8 Hz) reported by *Chang* et al.[5], however, the analogous splitting was not detected in the spectrum of chromone[10].

Assignments for the two remaining quaternary carbons (C-6a, C-10a) were readily achieved for **1** and **3** since C-10a was shifted upfield as experienced with 1-naphthol[17]. However, for **2** and **4** the assignments were more difficult. The signals overlapped in **4**, as confirmed through use of the "enhanced quaternary" technique[16]. The assignments for **2**

were made through consideration of relaxation effects, the least intense signal being assigned to C-10a with the smaller number of adjacent protons. The assignments could not be substantiated from the coupled spectrum since the peaks generally appeared as multiplets and were frequently obscured.

For the assignment of the methine signals, that for the residual pyrone ring carbon was first identified since the resonance was usually the farthest upfield and in the proton coupled spectrum showed additional fine quartet splittings. As in the case of the methyl carbons the couplings for **1** and **2** were larger than for **3** and **4** which again reflected the correlation of these interactions with the appropriate $^1H-^1H$ *vicinal* couplings[21].

The C-5 signal was readily identified by inspection of the proton coupled spectrum, since with the absence of an *ortho* ring oxygen, and of any *meta* aromatic hydrogens the signal appeared as a simple sharp doublet. The coupling in **1** was distinctly weaker than in **2–4**, presumably due to the adjacent methyl group, similar substituent effects upon $^1J_{CH}$ couplings have been observed for naphthalene derivatives[26].

The peak for C-6 could also be readily identified from the proton coupled spectrum, since it appeared as a doublet of very fine doublets, the *peri* coupling ($^3J \sim 5$ Hz) being much smaller than the other long range *meta* couplings[5]. The absorptions for **1** and **3** appeared upfield since the carbon was *para* to the ring oxygen. The final peak which could be definitively identified from the proton coupled spectrum was that for C-7. The assignment was facilitated by the considerably lower intensity of the peak doublets as a result of two long range couplings (*meta* and *peri*) being involved. However, due to signal overlap a complete analysis was not always possible.

The remaining signals for C-8, C-9 and C-10 were then allocated by reference to the spectra of suitable model compounds. For **1** and **3** the assignments were made by comparison with 1-naphthol[17], such that C-10 was far upfield with C-9 upfield of C-8. For the assignments of **2** the model compounds 4-methylphenanthrene[18] and 12-methylbenz(a)anthracene[19] were employed, thus C-10 was assigned as the downfield signal with C-8 and C-9 quite similar. For the assignment of **4** the model compounds used were phenanthrene-1,4-quinone[20] and benz(a)anthracene-7,12-dione[20] with the order C-10/C-8/C-9 pertaining in all cases.

An attempt to verify the assignments for C-8, C-9 and C-10 through consideration of long-range coupling effects was then made. All the peaks appeared as a wide spaced doublet, further split by a single long range *meta* coupling. It has been noted[26] that in naphthalene derivatives

the *meta* couplings which involve the β carbons are generally stronger than those at the α carbons, *viz* $J_{24} > J_{13}$. A similar relationship has been established[27] in the quinoline system such that $J_{68} > J_{86}$ and $J_{75} > J_{57}$. However, in the coumarin[4,5] and chromone[10] series such trends become less significant and the usual situation is such that J_{75} is the strongest coupling whilst J_{68} and J_{86} are often very similar. Application to **1** to **4** suggests that the following trends might be expected, either $J_{97} > J_{79}$ and $J_{8.10} > J_{10.8}$, or possibly $J_{8.10} > J_{10.8} > J_{97} \sim J_{79}$.

Extraction of the required coupling constant information was further hampered due to the close proximity of the peaks and by second order effects[29] at C-10 in **1** and **3**. Inspection of Table 2 shows that the expected trends are not strictly observed, although for those couplings that can be identified $J_{8.10}$ is generally the strongest and J_{79} the weakest for any given compound. More definitive conclusions must await further work in this area. It is possible that these general trends may not be applicable to three ring systems or that certain couplings could be additionally influenced by the *peri*-substitution pattern present. In this respect it should be recalled that an enhanced methyl coupling was observed in the *peri*-substituted compound **2**. The assignments of C-8, C-9 and C-10 made through comparison with the model compounds are therefore preferred.

Acknowledgement

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Experimental

All samples were recorded as dilute solutions in $CDCl_3$ using a Jeol JNM-FX-60 spectrometer operating in the pulsed *Fourier* Transform mode at 15 MHz, with broad band noise decoupling, pulse width 7 μs (45° pulse angle), pulse repetition rate 4 s, spectral width 2 500 Hz or 4 000 Hz with 8 K data points. For proton coupled spectra, the "Gated-1" alternatively pulsed sequence was used and the spectral width reduced to 1 000 Hz or 500 Hz to provide better digital resolution.

Samples were synthesised as described previously[1].

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