# Preparation and Some Spectral Properties of Benzo-fused 1,4-Dimethyl-2(1*H*)-quinolinones [1]



Keiichi Ito*, Junko Maruyama and Takako Shimamori

Hokkaido Institute of Pharmaceutical Sciences, Katsuraoka-cho, Otaru-shi, Hokkaido 047-02, Japan

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The preparation of the angular and linear isomers of benzo-fused 1,4-dimethyl-2(1*H*)-quinolinones **3a-5a** and their spectral data including $^{13}$C-nmr data are reported. Structural difference among **3a-5a** is confirmed from the proximity effect in $^{1}$H- and $^{13}$C-nmr data and from the uv spectral pattern.

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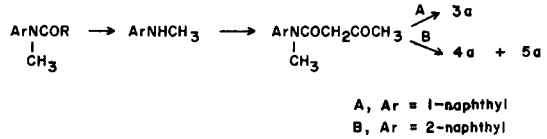
Although preparations and spectral properties of benzo-fused 4-methylcoumarins **3b-5b** are well documented [2] as an extension of naturally occurring coumarin chemistry, isosteric nitrogen analogs, 2(1*H*)-quinolinone derivatives, have not yet received attention in literature. The present paper describes the preparation of the angular (*ang*) and linear (*lin*) isomers of benzo-fused 1,4-dimethyl-2(1*H*)-quinolinones **3a-5a** in connection with comparison of their nmr and uv spectra with those of **3b-5b**.

*Ang* **3a** was readily prepared unambiguously from *N*-methyl-*N*-1-naphthylformamide in 45% total yield without purification of intermediates, according to the reported method [3] using diketene as an acetoacetylating agent. Attempted *N*-methylation of 4-methyl-2(1*H*)-benzo[*h*]quinolinone [4], as was successfully achieved for 4,5,7-trimethyl-2(1*H*)-quinolinone leading to **2a**, failed to give **3a** in reasonable yield presumably due to steric reason. Contrary to the facile cyclization of *N*-2-naphthylacetoacetamide into 1-methyl-3(4*H*)-benzo[*f*]quinolinone [4,5] in the presence of concentrated sulfuric acid, an attempt to prepare **4a** by a similar method starting from commercially available *N*-2-naphthylacetamide resulted in unexpected cyclization of the intermediate *N*-methyl-*N*-2-naphthylacetoacetamide to give *lin* **5a**, in addition to **4a** (**5a**:**4a** = 1.2:1), in 36% total yield. The isomeric structures of **3a**, **4a** and **5a** were confirmed as described below.

Since nmr studies with **3b** and **4b** were reported recently [2,6], we have performed nmr, especially $^{13}$C-nmr studies on **3a-5a** together with **2a** for comparison. Table 1 summarizes the $^{13}$C-nmr chemical shifts for **2a-5a** obtained in a conventional proton broad band decoupled mode of acquisition, and the selected $^{13}$C-$^{1}$H coupling constants, obtained through gated decoupling experiments, are collected in Table 2. Shift assignments were made by detailed analyses of the proton coupled splitting patterns, referring to the reported data describing the parent compound 1,4-dimethyl-2-(1*H*)-quinolinone **1a** [7], 1-methyl-2(1*H*)-quinolinone [8], and the related coumarin [9] and benzocoumarin system [6]. As for the aromatic system, the carbon signal appeared far downfield when it was bonded to nitrogen and far upfield when it was *ortho* to nitrogen, while significant long range coupling resulted from interaction with the ring hydrogen over three bonds.

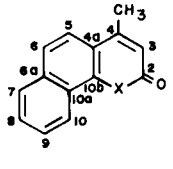
The peri-proximity effect in nmr spectroscopy, as discussed recently [6,10] on the benzo-fused coumarin derivatives, seems most appropriate for the structural differentiation between the *lin* and *ang* isomers **5a** and **3a**, **4a**, since this effect causes a marked deshielding of either *C*-or *N*-methyl proton and carbon signals depending upon spatial proximity. Thus, the *C*-methyl proton and carbon signals for **4a** appeared downfield from those for **3a** and **5a**. The *N*-methyl signals for **3a** followed the same trends.

Scheme

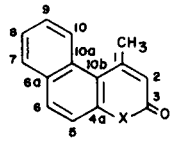



A, Ar = 1-naphthyl
B, Ar = 2-naphthyl

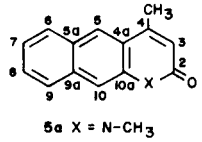
1a R = H, X = N-CH3
1b R = H, X = O
2a R = CH3, X = N-CH3
2b R = CH , X = O



3a X = N-CH3
3b X = O



4a X = N-CH3
4b X = O



5a X = N-CH3
5b X = O

Table 1

$^{13}$C-NMR Chemical Shifts [a] of **2a-5a**

| | C-2 | C-3 | C-4 | C-4a | C-5 | C-5a | C-6 | C-6a | C-7 | C-8 | C-9 | C-9a | C-10 | C-10a | C-10b | N-Me | C$^4$-Me |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **2a** [b] | 161.4 | 121.7 | 147.8 | 118.6 | 136.8 | — | 127.8 | — | 139.8 | 113.5 | — | — | — | 141.4 [c] | — | 29.9 | 25.7 |
| **3a** | 164.5 | 120.1 | 146.9 | 118.9 | 121.3 | — | 123.4 | 135.2 | 125.6 | 127.0 | 128.4 | — | 124.8 | 123.6 | 139.2 | 40.2 | 19.5 |
| **4a** | 122.6 | 161.0 | 147.3 [d] | 139.8 | 114.9 | — | 132.0 | 129.7 [f] | 125.2 | 124.6 | 128.9 | — | 127.0 | 130.6 [f] | 115.8 | 30.2 | 26.7 [e] |
| **5a** | 161.8 | 121.3 | 145.7 | 121.4 | 128.0 [g] | 128.2 | 127.0 [g] | — | 124.6 [f] | 124.7 [f] | 127.4 [g] | 133.8 | 110.0 | 136.9 | — | 28.9 | 18.8 |

[a] In ppm. [b] The resonances for $C_5$-Me and $C_7$-Me are 25.1 and 21.6 ppm, respectively. [c] C-8a. [d] C-1. [e] C$^1$-Me. [f] The corresponding values may be interchanged. [g] Assigned tentatively.

Table 2

$^{13}$C-$^1$H Coupling Constants [a] of **2a-5a**

| | **2a** | | **3a** | | **4a** | | **5a** | |
|---|---|---|---|---|---|---|---|---|
| | $^1$J | $^2$J, $^3$J | $^1$J | $^2$J, $^3$J | $^1$J | $^2$J, $^3$J | $^1$J | $^2$J, $^3$J |
| C-1 | ——— | | ——— | | ——— | C1H1Me = 6.1 | ——— | |
| C-2 | ——— | | ——— | [b] | C2H2 = 164.8 | C2H1Me = 6.1 | ——— | [b] |
| C-3 | C3H3 = 158.7 | C3H4Me = 6.1 | C3H3 = 160.0 | C3H4Me = 6.1 | ——— | | C3H3 = 166.0 | C3H4Me = 6.1 |
| C-4 | ——— | C4H4Me = 6.1 | ——— | C4H4Me = 6.1 | ——— | | ——— | C4H4Me = 6.1 |
| | | | | C4H3 = 2.4 | | | | |
| C-5 | ——— | C5H5Me = 6.1 | C5H5 = 161.1 | | C5H5 = 163.6 | | [b] | |
| C-6 | C6H6 = 148.9 | [b] | C6H6 = 163.6 | C6H7 = 4.9 | C6H6 = 162.4 | C6H7 = 6.1 | [b] | |
| C-7 | ——— | C7H7Me = 6.1 | [c] | | [c] | | C7H7 = 161.1 | C7H9 = 7.3 |
| C-8 | C8H8 = 157.5 | [b] | C8H8 = 162.4 | C8H10 = 8.5 | C8H8 = 162.4 | C8H10 = 8.5 | C8H8 = 161.2 | C8H6 = 7.3 |
| C-9 | ——— | | [c] | | [c] | | [b] | |
| C-10 | ——— | | C10H10 = 157.5 | C10H8 = 8.5 | C10H10 = 158.7 | C10H8 = 8.5 | C10H10 = 158.7 | C10H9 = 4.9 |
| N-Me | CH = 139.2 | ——— | CH = 141.6 | ——— | CH = 140.4 | ——— | CH = 140.4 | ——— |
| C4-Me | CH = 128.2 | C4MeH3 = 7.3 | CH = 128.2 | C4MeH3 = 6.1 | CH = 128.2 [d] | ClMeH3 = 7.3 | CH = 128.2 | C4MeH3 = 6.1 |
| C5-Me | CH = 127.0 | C5MeH6 = 6.1 | ——— | ——— | ——— | ——— | ——— | ——— |
| C7-Me | CH = 127.0 | [b] | ——— | ——— | ——— | ——— | ——— | ——— |

[a] In Hz: C-4a, 5a, 6a, 8a, 9a, 10a, 10b are not listed. [b] Complex multiplet, not analyzed. [c] Coupling obscured. [d] Cl-Me.

Table 3

Downfield Shift Values [a] of Methyl Groups

| Compound | $^1$H-NMR | | $^{13}$C-NMR | |
|---|---|---|---|---|
| | C-Me | N-Me | C-Me | N-Me |
| **2a** | 0.17 | −0.03 | 6.8 | 0.8 |
| **3a** | 0.01 | 0.24 | 0.6 | 11.1 |
| **4a** | 0.47 | 0.16 | 7.8 | 1.1 |
| **5a** | 0.11 | 0.06 | −0.1 | −0.2 |
| **2b** | 0.17 | | 7.6 | |
| **3b** | 0.01 | | 1.7 | |
| **4b** | 0.48 | | 8.8 | |
| **5b** | 0.12 | | 1.2 | |

[a] In ppm from the standard chemical shifts: δ 2.45 (C-$CH_3$), 3.70 (N-$CH_3$) and δ 18.9 (C-$CH_3$), 29.1 (N-$CH_3$) of **1a** for **2a-5a**; δ 2.42 ($CH_3$) and δ 17.5 ($CH_3$) of **1b** for **2b-5b**.

The downfield shift values (Δδ) of the two methyl groups estimated on the basis of the standard compound **1a** are listed in Table 3, which also contains the shift values of the *C*-methyl group in the analogous coumarin series **2b-5b** (4-methylcoumarin **1b** as the standard) for comparison. These data allow us easily to differentiate not only between the *lin* and *ang* isomers, but also between two *ang* isomers **3a** and **4a**. The proximity effect for **4a** and **4b**, in which one carbon forms a part of a fused benzene ring, was considerably larger than that for the simple peri methyl-methyl couples of **2a** and **2b**, respectively. The $^{13}$C-$^1$H coupling constants were also affected by the proximity effect. For instance, smaller $^1$J were observed for $C_{10}$-$H_{10}$ couples in the bay region of *ang* **3a** and **4a**. Also, enhanced long range coupling $^3$J to the pyron ring hydrogen (7.3 Hz) was experienced for the hindered *C*-methyl carbon of **2a** or **4a** when compared with the normal value for **1a**, **3a** or **5a** (6.1 Hz).

Table 4

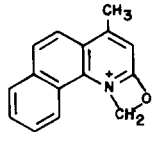
UV Spectral Data of **3a-5a** [a]

| Compound | λ max nm (ε × $10^{-4}$) | | |
|---|---|---|---|
| **3a** | 235.5 (2.32) | 271.5 (2.36) | 359.0 (0.83) |
| | | 281.5 (3.03) | |
| | | 306.5 (0.81) | |
| **4a** | 242.5 (7.31) | 301.5 (0.78) | 354.0 (0.78) |
| | 282.5 (1.22) | 313.5 (0.86) | 371.0 (0.76) |
| **5a** | 241.0 (5.06) | 266.0 (4.04) | 319.0 (0.95) |
| | 255.5 (3.58) | 277.0 (3.82) | 328.0 (1.23) |

[a] **1a**: 229.5 (4.24), 268.5 (0.67), 276.5 (0.63), 327.0 (0.68).

Ultraviolet spectra of **3a-5a** provide another pertinent data for the structural differentiation, as summarized in Table 4. Three main absorption bands of **1a** in ethanol, *i.e.*, 230 (band I), 269-277 (band II) and 327 nm (band III), could be observed for *lin* **5a** in a similar pattern, except that band I was shifted to the red and band II shifted bathochromically. On the contrary, uv spectra of *ang* **3a** and **4a** were rather complex and quite different from that of **5a**. Band III of **3a** and all three bands of **4a** were shifted to the red when compared with those of **1a**. Such spectral characteristics related to the isomeric difference in ring-fused structure resemble those already described [2] for **3b-5b**.

Infrared spectral data and mass spectral fragmentation patterns of **3a-5a** were comparable each other, as expected. However, the mass spectrum of **3a** is unique in that the most intense fragmentation peak appears at M-1 (m/e 222, base peak), which can be accounted for by facile thermal conversion of the sterically strained *N*-methyl group into a stable ion such as **6a** [11] with elimination of a hydrogen atom.



**6a**

## EXPERIMENTAL

All melting points were determined on a Yanaco micro melting point apparatus and are uncorrected. Infrared spectra were determined using a Hitachi 215 grating spectrophotometer. A Hitachi 200-10 spectrophotometer was employed to rercord uv spectra in ethanol. Mass spectra were taken on a Shimadzu LKB-900B spectrometer (direct inlet, at 70 eV). The $^1$H-nmr spectra were recorded at 100 MHz with a JEOL JNM-FX 100 spectrometer using tetramethylsilane as an internal standard and deuteriochloroform as a solvent unless otherwise stated. The $^{13}$C-nmr spectra were run on a JEOL JNM-FX 100 spectrometer operating in the pulse Fourier transform mode at 25 MHz, with sample concentration of *ca.* 15 w/v% in deuteriochloroform and a spectra width of 5000 Hz. Chemical shift values, measured relative to the central peak of the solvent (deuteriochloroform = 77.1 ppm) and corrected to internal tetramethylsilane, were reproducible within ± 0.05 ppm. The gated non-decoupled spectra with nuclear Overhauser effect for the determination of $J_{CH}$ were obtained setting the decoupler on during a pulse delay of 2.2 seconds and off during an acquisition time of 0.8 seconds.

1,4,5,7-Tetramethyl-2(1*H*)-quinolinone (**2a**).

4,5,7-Trimethyl-2(1*H*)-quinolinone was prepared from 3,5-dimethylaniline and diketene by the procedure similar to that described before [12], prisms from ethanol, mp 286-287°, 65% yield; ir (potassium bromide): 1655 cm$^{-1}$ (CO); $^1$H-nmr (DMSO-d$_6$): δ 2.28 (s, 3H, C$^7$-CH$_3$), 2.59 (s, 3H, C$^4$-CH$_3$), 2.65 (s, 3H, C$^5$-CH$_3$), 6.23 (s, 1H, C$^3$H), 6.79 and 6.96 (2s, 1H × 2, C$^6$H and C$^8$H), 11.45 (br s, 1H, NH).

To a solution of 4,5,7-trimethyl-2(1*H*)-quinolinone (3.6 g, 19 mmoles) in dry acetone (250 ml) methyl iodide (27 g, 19 mmoles) and anhydrous potassium carbonate (7.9 g, 57 mmoles) were added and the mixture was refluxed for 46 hours with vigorous stirring. The reaction mixture was cooled and concentrated *in vacuo*, and the residue was extracted with chloroform (100 ml × 3). Evaporation of the solvent afforded 2.8 g (72%) of crude crystals, which were recrystallized from acetonitrile to prisms, mp 140-141°; ir (potassium bromide): 1640 and 1659 cm$^{-1}$ (CO); $^1$H-nmr: δ 2.42 (s, 3H, C$^7$-CH$_3$), 2.62 (s, 3H, C$^4$-CH$_3$), 2.72 (s, 3H, C$^5$-CH$_3$), 3.67 (s, 3H, N-CH$_3$), 6.47 (s, 1H, C$^3$H), 6.85 and 7.05 (2s, 1H × 2, C$^6$H and C$^8$H).

*Anal.* Calcd. for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96. Found: C, 77.62; H, 7.55; N, 6.96.

1,4-Dimethyl-2(1*H*)-benzo[*h*]quinolinone (**3a**).

A sample of *N*-methyl-*N*-1-naphthylformamide (2.6 g, 14.1 mmoles), prepared as usual from *N*-1-naphthylformamide and methyl iodide with addition of sodium hydride in toluene, was hydrolyzed by refluxing with dilute hydrochloric acid (10%) for 3 hours. After cooling, the reaction solution was basified with sodium hydroxide solution (15%) and extracted with benzene (10 ml × 2). To the dried and ice-cooled benzene extracts was added diketene (1.2 g, 14.2 mmoles) dropwise with stirring, and then the mixture was heated to reflux. Another portion of diketene (0.6 g, 7.2 mmoles) was added after 4 hours, and refluxing was continued for total 13 hours with stirring. Concentration of the reaction solution gave an oily residue, which was added to concentrated sulfuric acid (5 ml) at 75° and heated for 30 minutes at 100°. The reaction mixture was poured into ice (*ca.* 150 g), neutralized with sodium hydroxide solution (15%) and extracted with chloroform (100 ml × 3). After drying over anhydrous magnesium sulfate, the chloroform solution was concentrated to afford 1.9 g of crude product. Chromatography over silica gel using a mixture of chloroform-carbon tetrachloride (1:1) as an eluent gave 1.4 g (45%) of pure **3a**, prisms from ethanol, mp 162-164°; ir (potassium bromide): 1658 cm$^{-1}$ (CO); ms: m/e 223 (M$^+$, 63), 222 (M-1, 100), 194 (17), 180 (11), 165 (7), 152 (14); $^1$H-nmr: δ 2.46 (s, 3H, C-CH$_3$), 3.94 (s, 3H, N-CH$_3$), 6.63 (s, 1H, C$^3$H), 7.42-7.88 (m, 5H, ArH), 8.26-8.36 (m, 1H, ArH).

*Anal.* Calcd. for $C_{15}H_{13}NO$: C, 80.69; H, 5.87; N, 6.27. Found: C, 80.77; H, 5.89; N, 6.39.

1,4-Dimethyl-3(4*H*)-benzo[*f*]quinolinone (**4a**) and 1,4-Dimethyl-2(1*H*)-benzo[*g*]quinolinone (**5a**).

A sample of *N*-methyl-*N*-2-naphthylacetamide (14.5 g, 72.5 mmoles), prepared as usual from *N*-2-naphthylacetamide and methyl iodide, was hydrolyzed and reacted with diketene by the similar procedure as described above for the preparation of **3a**. A portion of 6.5 g (77.4 mmoles) of diketene and refluxing time of 5 hours were enough for the reaction to afford crude *N*-methyl-*N*-2-naphthylacetoacetamide, which was treated with concentrated sulfuric acid by the similar manner to give 8.0 g of crude powder. This was shown to be a mixture of **4a** and **5a**, and was subjected to chromatography on silica gel (400 g) using a mixture of chloroform and benzene for graduent elution. Compound **5a** was obtained from the first fraction, weighing 4.3 g (27%), pale yellow needles from ethanol, mp 181-183°; ir (potassium bromide): 1653 cm$^{-1}$ (CO); ms: m/e 223 (M$^+$, 100), 194 (65), 180 (59), 165 (16), 152 (27); $^1$H-nmr: δ 2.56 (s, 3H, C-CH$_3$), 3.76 (s, 3H, N-CH$_3$), 6.62 (s, 1H, C$^3$H), 7.43-8.16 (m, 6H, ArH).

*Anal.* Calcd. for $C_{15}H_{13}NO$: C, 80.69; H, 5.87; N, 6.27. Found: C, 80.70; H, 5.82; N, 6.17.

The second fraction provided **4a**, 3.7 g (23%), plates from tetrahydrofuran-hexane, mp 128-130°; ir (potassium bromide): 1654 cm$^{-1}$ (CO); ms: m/e 223 (M$^+$, 100), 194 (63), 180 (32), 165 (16), 152 (25); $^1$H-nmr: δ 2.92 (s, 3H, C-CH$_3$), 3.86 (s, 3H, N-CH$_3$), 6.72 (s, 1H, C$^2$H), 7.49-8.02 (m, 5H, ArH), 8.59-8.67 (m, 1H, ArH).

*Anal.* Calcd. for $C_{15}H_{13}NO$: C, 80.69; H, 5.87; N, 6.27. Found: C, 80.69; H, 5.87; N, 6.27.

Acknowledgement.

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