# Carbon-13 and Proton NMR Spectra of 1(2H)-Isoquinolinone, 1(2H)-Phthalazinone, 4(3H)-Quinazolinone and their Substituted Derivatives

S. L. SPASSOV (to whom correspondence should be addressed) Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences, 1113 Sofia. Bulgaria I. A. ATANASSOVA and M. A. HAIMOVA Department of Chemistry, University of Sofia, 1126 Sofia, Bulgaria The <sup>13</sup>C NMR chemical shifts, one-bond and some long-range <sup>13</sup>C-<sup>1</sup>H coupling constants and the <sup>1</sup>H NMR chemical shifts for isoquinolinone, phthalazinone, quinazolinone and their derivatives con-

taining  $CH_3$ , COOH, COOCH<sub>3</sub> and  $CH_2COOH$  substituents in the hetero-ring are reported. The NMR data are in agreement with the lactam structure for all compounds studied; no evidence for the detectable presence of other tautomers was obtained.

#### **INTRODUCTION**

In a previous paper,<sup>1 13</sup>C NMR data for *N*-methyl-1(2*H*)-isoquinolinone and some of its substituted derivatives were reported. Although the 1(2*H*)-isoquinolinones have been extensively studied by UV, IR and <sup>1</sup>H NMR spectroscopy, mainly in connection with their possible tautomerism,<sup>2</sup> there

are almost no <sup>13</sup>C NMR data published for such compounds. <sup>13</sup>C NMR data for substituted phthalazines and quinazolines are also scarce, whereas other fused-ring diazaheterocycles, such as benzimidazoles and quinoxalines, have received more attention.<sup>3</sup>

In this paper, the <sup>13</sup>C chemical shifts and the one-bond and some long-range <sup>13</sup>C-<sup>1</sup>H coupling constants for 1(2H)-isoquinolinone, 1(2H)-phthalazinone, 4(3H)quinazolinone and some of their substituted derivatives are reported. Proton chemical shift data obtained at 250 MHz are also included.

# **RESULTS AND DISCUSSION**

The  ${}^{13}$ C NMR chemical shifts and one-bond carbon-hydrogen coupling constants are given in Tables 1 and 2. Some of the long-range  ${}^{13}$ C- ${}^{1}$ H coupling constants which could be determined and assigned are presented in Table 3. The proton chemical shifts are reported in Table 4; their assignment was confirmed by  ${}^{1}$ H- ${}^{1}$ H selective decoupling experiments.

#### **Isoquinolinones 1-6**

For isoquinolinone (1), the assignment of all protonated carbon signals was achieved unequivocally by two-dimensional  ${}^{1}H{}^{-13}C$  correlation based on the already identified proton signals. The assignments of C-9,10 were achieved as described in Ref. 1. The  ${}^{13}C$ chemical shifts obtained for 1 (Table 1) are close to those reported for the N-methyl derivative,<sup>1</sup> except for C-3, which is shielded by ca 4 ppm in 1. On the other hand, the C-3,4 signals in 1 are more than 10 ppm upfield with respect to the corresponding C atoms in 1-methoxyisoquinoline (7), used as a model for the aromatic tautomer of 1. This confirms the oxo (lactam) structure of isoquinolinone (1) and its analogues 2-6, in agreement with results based on other methods.<sup>2</sup>

For the substituted isoquinolinones 2-6, similar trends are observed to those for their N-methyl analogues.<sup>1</sup> For the benzene ring carbons, the substituent effect is more pronounced for a substituent in the 3-position (compounds 2 and 4), where the deshielding of C-5.7.9 by 2-3 ppm can be attributed to an increased electron withdrawal due to substituent conjugation. The magnitude of the effect is almost the same as in cinnamic acid and its esters, in contrast to styrene. In view of the present conclusions, as well as other recent results,<sup>4</sup> the C-7,8 chemical shift values for the 3-COOR'-substituted  $(R = H, CH_3)$  isocoumarins and isoquinolinones reported in Ref. 1 may have to be interchanged.

In addition to the chemical shift of C-1, the isoquinolinone ring system is also characterized by the high values (compared with protonated benzene carbons) of  ${}^{1}J$ ( ${}^{13}C^{1}H$ ) for C-3 (178–182 Hz) and, to some extent, also for C-4 (167–172 Hz). For the long-range couplings (Table 3), the slightly smaller  ${}^{3}J({}^{13}C^{1}H)$  value for C-5 (6–7 Hz), compared with those for C-6,7,8 (7–8 Hz), may be of some diagnostic value.

Table 1. <sup>13</sup>C NMR data for 1(2H)-isoquinolinones 1-6 and 1-methoxyisoquinoline (7), with <sup>13</sup>C chemical shifts, and one-bond <sup>13</sup>C-<sup>1</sup>H coupling constants (Hz) in parentheses

 $\mathbf{R}_{2}$ 

|                |       |                |                             |       |                    |       | _1 <sup>2</sup> NH |         |         |         |         |                 |       |       |
|----------------|-------|----------------|-----------------------------|-------|--------------------|-------|--------------------|---------|---------|---------|---------|-----------------|-------|-------|
|                |       |                |                             |       |                    | 8     | Ĭ                  |         |         |         |         |                 |       |       |
| Compound       | R1    | R <sup>2</sup> | Solvent                     | CH₃   | CO(R)              | C-1   | С-3                | C-4     | C-5     | C-6     | C-7     | C-8             | C-9   | C-10  |
| 1              | н     | н              | DMSO-d <sub>6</sub>         | _     | _                  | 101.8 | 128.6              | 104.5   | 126.0   | 132.1   | 126.1   | 126.5           | 125.9 | 137.8 |
| -              |       |                | <b>D</b> 1100 /             | 50.0  | 404.0              |       | (180.0)            | (168.0) | (163)   | (161.0) | (163.5) | (162.5)         | 107.0 | 105 7 |
| 2              | COOCH | з Н            | DMS0- <i>a</i> <sub>6</sub> | 52.8  | 161.8              | 161.3 | 128.9              | (172.0) | (163.5) | (162.0) | (163.0) | (163.5)         | 127.9 | 135.7 |
| 3              | н     | COOCH3         | DMSO-d <sub>6</sub>         | 51.4  | 165.1              | 161.7 | 137.3              | 104.7   | 124.7   | 133.0   | 126.8ª  | 1 <b>27</b> .0ª | 125.2 | 134.6 |
|                |       |                |                             |       |                    |       | (181.0)            |         | (166.0) | (161.5) | (163.0) | (164.0)         |       |       |
| 4              | COOH  | н              | DMSO-d <sub>6</sub>         |       | 162.7              | 161.2 | 129.7              | 109.6   | 128.1   | 132.8   | 128.7   | 126.8           | 127.7 | 135.8 |
|                |       |                |                             |       |                    |       |                    | (171.5) | (163.5) | (162.0) | (164.0) | (164.0)         |       |       |
| 5              | н     | COOH           | DMSO-d <sub>6</sub>         | —     | 166.4              | 161.7 | 137.4              | 105.3   | 125.1   | 132.8   | 126.5ª  | 126.9ª          | 125.3 | 135.0 |
|                |       |                |                             |       |                    |       | (181.0)            |         | (164.5) | (161.5) | (163.5) | (163.5)         |       |       |
| 6 <sup>b</sup> | н     | н              | DMSO-d <sub>6</sub>         | 49.8° | 169.7 <sup>d</sup> | 161.1 | 133.5              | 104.7   | 126.1   | 132.3   | 126.6ª  | 126.8ª          | 125.1 | 137.1 |
|                |       |                |                             |       |                    |       | (182.0)            | (169.0) | (162.5) | (161.5) | (163.0) | (163.5)         |       |       |
| 7°             | 1-Me  | thoxy-         | CDCl <sub>3</sub>           | 53.6  |                    | 161.0 | 139.7              | 114.9   | 126.0   | 130.3   | 126.5   | 124.1           | 119.8 | 137.9 |
|                | isoqu | inoline        |                             |       |                    |       | (179.0)            | (163.0) | (161.0) | (160.5) | (161.5) | (163.5)         |       |       |

\* Values may be interchanged.

<sup>b</sup> CH<sub>2</sub>COOH substituents at the N atom.

° CH<sub>2</sub>.

a COOH.

<sup>•</sup> The chemical shift values are very close to those reported for 1-ethoxyisoquinoline.<sup>34</sup>

| Table 2. | <sup>13</sup> C NMR | data for                        | phthalazinones   | 8-15 and   | quinazolinones | 16-19* | <b>solutions</b> i | in DN | MSO-d <sub>6</sub> , | with | <sup>13</sup> C | chemical | shifts | (ppm) | and |
|----------|---------------------|---------------------------------|------------------|------------|----------------|--------|--------------------|-------|----------------------|------|-----------------|----------|--------|-------|-----|
|          | one-bond            | <sup>13</sup> C- <sup>1</sup> H | coupling constar | ts (Hz) in | parentheses    |        |                    |       |                      |      |                 |          |        |       |     |

# $\begin{array}{c} \mathbf{R}_{2} \\ \mathbf{R}_{3} \\ \mathbf{R}_{4} \\ \mathbf{R}_{4} \\ \mathbf{R}_{4} \\ \mathbf{R}_{4} \\ \mathbf{R}_{1} \\ \mathbf{R}_{1} \\ \mathbf{R}_{1} \\ \mathbf{R}_{1} \\ \mathbf{R}_{2} \\ \mathbf{R}_{1} \\ \mathbf{R}_{1} \\ \mathbf{R}_{2} \\ \mathbf{R}_{1} \\ \mathbf{R}_{1} \\ \mathbf{R}_{2} \\ \mathbf{R}_{2} \\ \mathbf{R}_{1} \\ \mathbf{R}_{2} \\ \mathbf{R}_{2} \\ \mathbf{R}_{2} \\ \mathbf{R}_{1} \\ \mathbf{R$

|          |   |   |         |     |                |                   |       | Ŷ       |         |                |         |                    |         |       |       |
|----------|---|---|---------|-----|----------------|-------------------|-------|---------|---------|----------------|---------|--------------------|---------|-------|-------|
| Compound | х | Y | R       | R,  | R <sub>2</sub> | R,R1,R2           | C-1   | C-3     | C-4     | C-5            | C-6     | C-7                | C-8     | C-9   | C-10  |
| 8        | Ν | С | н       |     | н              |                   | 159.7 |         | 138.3   | 131.7          | 133.6   | 126.7              | 125.4   | 127.6 | 129.9 |
|          |   |   |         |     |                |                   |       |         | (186.5) | (162.5)        | (164.0) | (164.5)            | (163.5) |       |       |
| 9        | N | С | н       |     | CH3            | 18.3              | 159.4 |         | 143.1   | 131.3          | 133.3   | 125.4              | 125.7   | 127.3 | 129.7 |
|          |   |   |         |     | -              |                   |       |         |         | (163)          | (163.0) | (163.5)            | (164.5) |       |       |
| 10       | Ν | С | н       |     | COOH           | 164.8             | 159.6 |         | 136.5   | 131.8          | 134.0   | 125.9              | 126.3   | 127.5 | 127.8 |
|          |   |   |         |     |                |                   |       |         |         | (164.0)        | (163.5) | (164.5)            | (164)   |       |       |
| 11       | Ν | С | н       |     | CH₂COOH        | 38.2              | 159.5 |         | 141.4   | 131.5          | 133.5   | 125.5              | 125.9   | 127.5 | 129.6 |
|          |   |   |         |     |                | 171.4             |       |         |         | (164)          | (163.5) | (164)              | (164)   |       |       |
| 12       | Ν | С | CHa     |     | COOH           | 50.6              | 158.5 |         | 135.7   | 31.8           | 133.5   | 126.0 <sup>°</sup> | 126.1°  | 126.8 | 127.4 |
|          |   |   |         |     |                | 164.3             |       |         |         | (164.0)        | (163.5) | (164)              | (164)   |       |       |
| 13       | Ν | С | CH₃     |     | CH₂COOH        | 38.1 <sup>b</sup> | 158.4 |         | 141.0   | 131.7          | 133.1   | 125.5              | 126.0   | 127.0 | 129.1 |
|          |   |   |         |     |                | 171.2             |       |         |         | (164.0)        | (164.0) | (164.0)            | (164.5) |       |       |
|          |   |   |         |     |                | 38.7 <sup>b</sup> |       |         |         |                |         |                    |         |       |       |
| 14       | Ν | С | CH₂COOH |     | н              | 52.5              | 158.5 |         | 138.0   | 132.1          | 133.6   | 126.9              | 125.6   | 126.9 | 129.5 |
|          |   |   | -       |     |                | 169.3             |       |         | (188.0) | (162.5)        | (164.5) | (165.0)            | (164)   |       |       |
| 15       | Ν | С | CH₂COOH |     | CH₃            | 18.3              | 158.3 |         | 143.3   | 131.7          | 133.5   | 125.6              | 126.0   | 126.7 | 129.4 |
|          |   |   | _       |     | -              | 52.3              |       |         |         | (164)          | (163.5) | (164.5)            | (164.5) |       |       |
|          |   |   |         |     |                | 169.3             |       |         |         |                |         |                    |         |       |       |
| 16       | С | Ν | н       | н   |                | _                 | 161.4 | 145.8   | —       | 126.2          | 134.6   | 127.0              | 127.3   | 122.8 | 148.9 |
|          |   |   |         |     |                |                   |       | (204.5) |         | (163.0)        | (163.0) | (164.5)            | (164.0) |       |       |
| 17       | С | Ν | н       | СНз | <u> </u>       | 21.3              | 161.6 | 154.1   |         | 125.6          | 134.0   | 125.6              | 126.5   | 120.6 | 148.9 |
|          |   |   |         | -   |                |                   |       |         |         | (163.0)        | (163)   | (164.5)            | (163.0) |       |       |
| 18       | С | Ν | CH₂COOH | н   |                | 47.1              | 160.1 | 148.0   |         | 125.9          | 134.4   | 127.1°             | 127.2°  | 121.3 | 147.9 |
|          |   |   |         |     |                | 169.2             |       | 207.5   |         | (164.0)        | (163.0) | (165.0)            | (164.0) |       |       |
| 19       | С | Ν | CH₂COOH | CH₃ |                | 22.7              | 161.0 | 154.8   |         | <b>126</b> .1° | 134.3   | 126.4°             | 126.5°  | 119.5 | 147.0 |
|          |   |   |         |     |                | 45.3              |       |         |         | (163.5)        | (164.0) | (164.5)            | (164)   |       |       |
|          |   |   |         |     |                | 169.4             |       |         |         |                |         |                    |         |       |       |

\* The numbering of quinazolinones is non-systematic for convenience.

<sup>b</sup> Assignment of CH<sub>2</sub> and CH<sub>3</sub> unknown, owing to partial overlap with the DMSO-d<sub>6</sub> signal.

<sup>c</sup> Values may be interchanged.

In the case of the <sup>1</sup>H chemical shifts, the order  $\delta(H-8) > \delta(H-6) > \delta(H-7)$ , also valid for isocoumarins and N-methylisoquinolinones,<sup>1.5</sup> was observed. The position of the H-5 signal is variable, reaching 8.8 ppm in the case of the 4-substituted compounds **3** and **5**, evidently owing to the anisotropic effect of the COOR' (R'=H, CH<sub>3</sub>) group.

#### Phthalazinones 8-15

No  ${}^{13}$ C NMR data for phthalazinones have been reported to our knowledge. The closest systems studied include phthalazine itself<sup>5</sup> and compound **20**.<sup>6</sup>



For the assignment of the  ${}^{13}C$  signals (Table 2), C-4 was recognized by its high  ${}^{1}J({}^{13}C{}^{1}H)$  value, C-5 by the additional vici-

nal coupling with H-4 and C-6 by its chemical shift, which is the least sensitive to substituent effects in all compounds 1-19. Differentiation between C-7 and C-8 was achieved by selective decoupling. The quaternary carbons C-9, and C-10 were identified on the basis of the long-range <sup>1</sup>H-<sup>13</sup>C coupling pattern. The slightly distorted C-8 signal form observed for most phthalazinone derivatives was useful for its identification. As can be seen from Table 2. the <sup>13</sup>C chemical shifts for C-1 in phthalazinones (158.3-159.7 ppm) differ from those for isoquinolinones, N-methylisoquinolinones and quinazolinones (161-163 ppm).<sup>1,4</sup> Another distinction from the compounds mentioned is that the C-5 signal position in phthalazinones is practically unaffected by 4-substituents.

In the <sup>1</sup>H NMR spectra of phthalazinones, H-5,6,7 give closely packed complex multiplets at 250 MHz, with the exception of compounds 10 and 12, where H-5 is again strongly deshielded by a 4-COOH. The H-8 signal (near doublet) at 8.2-8.3 ppm is characteristic.

No NMR evidence was found for the detectable presence of a lactim tautomer in

phthalazinones, in agreement with  $IR^7$  and  $UV^8$  results.

#### Quinazolinones (16-19)

For comparative purposes, the atomic numbering in Tables 2-4 differs from that usually employed for 4(3H)-quinazolinones. Published <sup>13</sup>C NMR data (chemical shifts only) are limited to quinazolinone (16) and some 2- and 3-alkyl derivatives (including 17),<sup>9</sup> and some tricyclic 3,4-dihydro analogues.<sup>10</sup> The <sup>13</sup>C chemical shifts for 16 and 17 are in satisfactory agreement with those given in Ref. 9, with the exception of the carbonyl signal in 16 (reported value 165.7 ppm<sup>9</sup>). For this type of compound the most characteristic signal is that for C-3, with its high <sup>1</sup>J(<sup>13</sup>C<sup>1</sup>H) value and/or distinctive long-range coupling pattern.

The <sup>1</sup>H NMR spectra of quinazolinones 16-19 resemble those of isoquinolinones 1-6, the chemical shift order of the benzenoid protons being the same. The low-field singlet for H-3 at 8.1-8.4 ppm is characteristic.

Again, no evidence was obtained for the

| REFERENCE | DATA |
|-----------|------|
|-----------|------|

| Table 3.  | Some long          | -range <sup>13</sup> C- | <sup>1</sup> H couplir | ig constants       | (Hz) for | compound 1 | l-19ª   | · ·  |
|-----------|--------------------|-------------------------|------------------------|--------------------|----------|------------|---------|--|
| Compound  | C-1                | C-3                     | C-4                    | C-5                | C-6      | C-7        | C-8     | Others   |
| 1         | 7.0 H-3<br>3.5 H-8 | 4.5 H-4                 | 3.5 H-3<br>3.5 H-5     | 4.0 H-4            | 8.0 H-8  | 8.0 H-5    | 7.0 H-6 |  |
| 2         | 3.0 H-8            | 1.5 H-4                 | 5.0 H-5                | 4.5 H-4<br>7.0 H-7 | 8.0 H-8  | 7.5 H-5    | 7.0 H-6 | ${}^{3}J(COOCH_{3}) = 4.0$<br>${}^{3}J(COOCH_{3}, H = 4)$<br>= 4.0 |
| 3         |                    |                         |                        | 7.0 H-7            | 8.0 H-8  | 8.0 H-5    | 7.5 H-6 |  |
| 4         | 3.0 H-8            | 1.5 H-4                 | 4.5 H-5                | 4.0 H-4<br>7.0 H-7 | 8.0 H-8  | 8.0 H-5    | 7.0 H-6 | <sup>3</sup> J(COOH, H-4) =<br>4.0                                 |
| 5         |                    |                         |                        | 6.0 H-7            | 8.0 H-8  | 8.0 H-5    | 8.0 H-6 |  |
| 6         |                    | 4.5 H-4                 | 3.0 H-3<br>3.0 H-5     | 4.0 H-4<br>7.0 H-7 | 8.0 H-8  | 7.5 H-5    | 7.0 H-6 | <sup>2</sup> J(CH <sub>2</sub> COOH) =<br>6.0                      |
| 7         |                    | 3.0 H-4                 | 7.0 H-3<br>4.6 H-5     | 4 H-4<br>7 H-7     | 8.0 H-8  | 8.0 H-5    | 6.5 H-6 |  |
| 8         | 3.5 H-8            |                         |                        |                    | 8.5 H-8  | 7.0 H-5    |         |  |
| 9         |                    |                         |                        | 7.0 H-7            | 8.0 H-8  | 7.0 H-5    |         |  |
| 10        |                    |                         |                        | 8.0 H-7            | 8.0 H-8  | 8.0 H-5    | 8.0 H-6 |  |
| 11        |                    |                         |                        | 7.0 H-7            | 8.0 H-8  |            |         | <sup>2</sup> J(CH <sub>2</sub> COOH) = 8                           |
| 12        |                    |                         | 3 H-5                  | 8.5 H-7            | 8.0 H-8  |            |         |  |
| 13        |                    |                         |                        | 7.0 H-7            | 8.0 H-8  | 7.5 H-5    |         | <sup>2</sup> J(CH <sub>2</sub> COOH) =<br>7.0                      |
| 14        |                    |                         |                        |                    | 8.0 H-8  | 7.5 H-5    |         | <sup>2</sup> J(CH <sub>2</sub> CHOH) =<br>6.0                      |
| 15        | 3.0 H-8            |                         |                        |                    | 8.0 H-8  | 7.0 H-5    |         | <sup>2</sup> J(CH <sub>2</sub> COOH) =<br>5.5                      |
| 16        |                    |                         |                        | 8.0 H-7            | 8.5 H-8  | 8.0 H-5    | 8.0 H-6 |  |
| 17        | 3.0 H-8            | 7.0 CH <sub>3</sub>     |                        |                    | 8.5 H-8  |            | 7.5 H-6 |  |
| 18        | 4 H-8              | 4.5 CH <sub>2</sub>     |                        | 7.5 H-7            | 8.5 H-8  |            |         | <sup>2</sup> J(CH <sub>2</sub> COOH) ≔<br>6.0                      |
| 19        |                    |                         |                        | 7.5 H-7            |          |            |         | $^{2}J(CH_{2}COOH) =$  |
|           |                    |                         |                        | 8.5 H-8            |          |            |         | 6.0  |
| * See Tal | ole 2, foot        | tnote a.                |                        |                    |          |            |         |  |

presence of other tautomers, in accordance with previous data.<sup>11</sup>

## EXPERIMENTAL

The <sup>13</sup>C and <sup>1</sup>H NMR spectra were obtained at ambient temperature (297 K) on a Bruker WM-250 FT spectrometer equipped with an ASPECT 2000 computer at 62.9 and 250.1 MHz, respectively. Typical conditions for the <sup>13</sup>C spectra were as follows: memory size, 16K; pulse width, ca 30°; relaxation delay, 2s; and digital resolution, 2 Hz (0.5 Hz for the proton-coupled spectra). The concentrations of the solutions were 0.5-1 M and TMS was used as the internal standard. The  ${}^{13}C{}^{-1}H$  coupling constants were obtained from the protoncoupled <sup>13</sup>C spectra (gated-decoupling technique) by first-order analysis, and their signs were not determined. The two-dimensional <sup>1</sup>H-<sup>13</sup>C correlation was performed using the standard Bruker programme (DISNMR Manual, 1983). The optimal parameters were similar to those employed in Ref. 35.

The preparative methods and the physical properties of most of the compounds studied are summarized in Table 4.

### 1(2H)-Isoquinolinone (1)

Isoquinoline N-oxide (5 g) and acetic anhydride (100 ml) were boiled for 6 h and

the hot mixture was poured over 100 g of ice and then neutralized with solid KOH. After filtration and dilution with 100 ml of cold water, crystalline 1(2H)-isoquinolinone (4 g) was obtained and recrystallized from benzene.

# 3-Methoxycarbonyl-1(2H)-isoquinolinone (2)

3-Carboxy-1(2H)-isoquinolinone (1.89 g, 10 mmol) was suspended in 10 ml of methanol, 3.4 ml (20 mmol) of N-ethyldiisopropylamine and 1.2 ml (12 mmol) of dimethyl sulphate were added and the mixture was heated for 15 min on a steam-bath. After addition of 5 ml of water and 5 ml of 2N HCl the crude ester (1.90 g, 92%) was filtered and recrystallized from methanol.

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| Table                         | 4. Methods of preparation,  | melting points and <sup>4</sup> H NM                 | IK data for compounds 1–19"  |
|-------------------------------|---|--|--|
| Compou                        | ind Method of preparation<br>and (lit. m.p., °C)                        | M.p. (°C)<br>(solvent)                               | <sup>1</sup> H NMR parameters (250 MHz, in DMSO-d <sub>6</sub> ) <sup>b.c</sup>  |
| ۲                             | See text (208) <sup>12</sup>  | 208-210  | 6.53d ( <i>J</i> = 7.3, H-4), 7.16d ( <i>J</i> = 7.3, H-3), 7.45m (H-7), 7.61m (H-5), 7.65m (H-6), 8.18m (H-8), 11.27b (NH)              |
| 7                             | See text (158–159.5) <sup>13</sup>                                      | (benzene)<br>157–159                                 | 3.85s (CH <sub>°</sub> O), 7.39s (H-4), 7.62m (H-7), 7.75m (H-6), 7.83m (H-5), 8.22m (H-8), 11.19b (NH)                                  |
| ო                             | Lit. <sup>14</sup> (240–242) <sup>15</sup>                              | (methanol)<br>240–242                                | 3.80s (CH <sub>3</sub> O), 7.54m (H-7), 7.79m (H-6), 8.01s (H-3), 8.23m (H-8), 8.71m (H-5), 11.88b (NH)                                  |
| 4                             | Lit. <sup>16</sup> (327–330) <sup>16</sup>                              | (methanol)<br>328–330                                | 7.39s (H-4), 7.62m (H-7), 7.76m (H-6), 7.87m (H-5), 8.21m (H-8), 10.91b (NH)   |
| I                             | •   | (acetic acid)  |  |
| ŝ                             | Alkaline hydrolysis<br>of 3 (297) <sup>17</sup>                         | 295–297<br>(acetic acid)                             | 7.53m (H-7), 7.78m (H-6), 8.03s (H-3), 8.24m (H-8), 8.83m (H-5), 11.80b (NH)   |
| 9                             | Lit. <sup>18</sup>  | 247-248  | <b>4.69s</b> (CH <sub>2</sub> N), 6.61d ( $J = 7.3$ , H-4), 7.44d ( $J = 7.3$ , H-3), 7.49m (H-7), 7.64m (H-5), 7.70m (H-6), 8.20m (H-8) |
| 7                             | Lit <sup>.12</sup> (b.n. 135–   | (ethanol-diethyl ether<br>b.n. 135-139 °C            | )<br>In CDCL-:4 11s (CH-O). 7 16d (J = 5.9, H-4). 7.47m (H-7). 7.59m (H-6). 7.67m (H-5). 7.99d (J = 5.9, H-3). 8.21m (H-8)               |
|                               | 136 °/21 mmHg)  | 21 mmHg  |  |
| œ                             | Lit. <sup>19</sup> (184) <sup>19</sup>                                  | 183–185<br>//  | 7.7–7.9m (H-5, 6, 7), 8.20m (H-8), 8.34s (H-4)   |
| ດ                             | Lit. <sup>20</sup> (221–223) <sup>20</sup>                              | (etnanoi)<br>221–223                                 | 2.50s (CH <sub>3</sub> ), 7.7–8.0m (H-5, 6, 7), 8.22m (H-8), 12.40b (NH)   |
| ;                             |   | (ethanol)  |  |
| 10                            | Lit. <sup>41</sup> (22 <del>9–</del> 230) <sup>44</sup>                 | 230-231<br>(athenol)                                 | 7.8–8.0m (H-6, 7), 8.27m (H-8), 8.55m (H-5)  |
| 11                            | Lit. <sup>23</sup> (165 decomp.) <sup>23</sup>                          | 164-165  | 3.95s (CH <sub>2</sub> ), 7.7–8.0m (H-5, 6, 7), 8.26m (H-8)  |
| 12                            | Lit. <sup>24</sup> (237) <sup>24</sup>                                  | (ethanol, decomp.)<br>235–237                        | 3.77s (CH <sub>3</sub> N), 7.87m (H-7), 7.96m (H-6), 8.30m (H-8), 8.54m (H-5)  |
| 13                            | Lit. <sup>25</sup> (195) <sup>25</sup>                                  | (acetic acid)<br>193–195                             | 3.69s (CH_N) 3.97s (CH_) 7.8–7.9m (H-5. 6.7).8.28m (H-8)   |
| 2                             |   | (ethanol, decomp.)                                   |  |
| 14                            | Alkaline hydrolysis   | 233-235  | 4.82s (CH <sub>2</sub> N), 7.8–8.0m (H-5, 6, 7), 8.24m (H-8), 8.44s (H-4)  |
| 15                            | or etnyl ester <sup>rud</sup><br>Lit. <sup>20</sup> (255) <sup>20</sup> | (etnanol)<br>253-255                                 | 2.52s (CH <sub>3</sub> ), 4.76s (CH <sub>2</sub> N), 7.8–8.0m (H-5, 6, 7), 8.25m (H-8)   |
| 16                            | Lit. <sup>27</sup> (212) <sup>27</sup>                                  | (acetic acid)<br>211–212                             | 7.50m (H-7), 7.65m (H-5), 7.80m (H-6), 8.10s (H-3), 8.11m (H-8)  |
| 17                            | Lit. <sup>28</sup> (234) <sup>28</sup>                                  | (ethanol)<br>234–235                                 | 2.33s (CH <sub>3</sub> ), 7.43m (H-7), 7.55m (H-5), 7.75m (H-6), 8.05m (H-8), 12.18b (NH)  |
| 18                            | Lit. <sup>29</sup> (22 <del>8–</del> 230,                               | (ethanol)<br>228–230                                 | 4.73s (CH <sub>5</sub> N), 7.56m (H-7), 7.70m (H-5), 7.84m (H-6), 8.14m (H-8), 8.36s (H-3)   |
| :                             | decomp.) <sup>28</sup>  | (acetic acid, decomp.)                               |  |
| 6L                            | Analogously to lit. <sup>30</sup><br>(263) <sup>31</sup>                | 263–265<br>(acetic acid)                             | 2.12 (CH <sub>3</sub> ), 4.83s (CH <sub>2</sub> N), 7.5–7.8m (H-5, 6, 7), 8.0/m (H-8)  |
| <sup>a</sup> See 1<br>b 60 MI | footnote a in Table 2.<br>Hz data (no assignment of                     | f aromatic protons): 1 an                            | d 2, Ref. 15; 2, Ref. 13; 5, Ref. 32; 8, Ref. 11.  |
| <sup>c</sup> Our c            | data differs significantly fit spectrum $m/z$ 204(m <sup>+</sup> );     | rom those reported for 1<br>IR spectrum (Nujol) 1640 | 7 and 19 at 60 MHz. <sup>33</sup><br>) (amide Co), 1730 (acid CO), 3500 (OH) cm <sup>−1</sup> .  |

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