obtained, which after recrystallization from ether afforded 305 mg (27%) of white needles, m.p. 78–80 °C.

Anal. Calcd. for $C_8H_8N_2$: C, 72.73; H, 6.06; N, 21.22. Found: C, 73.01; H, 5.72; N, 21.37.

## Acknowledgment

One of us (P. G. Riley) acknowledges the award of a research scholarship by the Science Research Council, London, England.

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# Nuclear magnetic resonance spectrum and deuteration of porphobilinogen lactam and its derivatives[1]

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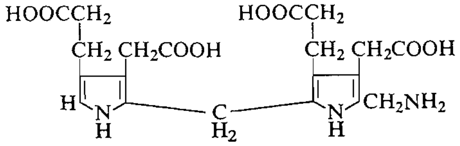
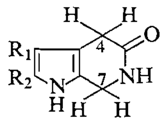
Derivatives of porphobilinogen are distinguished from those of its lactam in that the $C_4$- and $C_7$-protons of the latter show homoallylic coupling, $J_{4,7}$ = 2.5–3.0 Hz (150°) and the $C_4$-protons are exchangeable in alkaline solution.

Canadian Journal of Chemistry, 47, 3259 (1969)

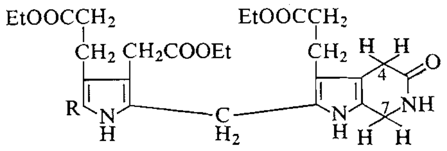
As will be reported elsewhere (1), the very labile dipyrryl-methane **1** was synthesized for biogenetic studies as a reasonably stable potassium salt. As obtained by the hydrolysis of **8**, it was difficult to characterize, and the usual methods did not clearly show that the lactam ring had been opened. We now report an examination of model porphobilinogen derivatives **2–10** (1–3) showing that, in lactam but not in open forms, the $C_4$- and $C_7$-protons show homoallylic coupling, $J_{4,7}$ = 2.5–3.0 Hz (150°) and the $C_4$-protons are exchangeable; in alkaline $D_2O$, this exchange is faster than ring-opening.



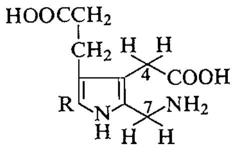
**1**



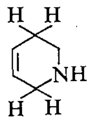
| | $R_1$ | $R_2$ |
|---|---|---|
| **2** | $CH_2CH_2COOEt$ | COOEt |
| **3** | $CH_2CH_2COOEt$ | H |
| **4** | $CH_2CH_2COOH$ | COOH |
| **5** | $CH_2CH_2COOH$ | H |



**6** R = $COOCH_2C_6H_5$
**7** R = COOH
**8** R = H



**9** R = COOH
**10** R = H (porphobilinogen)



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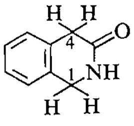

**12**

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[1] NRCC No. 10750.

[2] NRCC Postdoctorate Fellow, 1965–1967. Present address: Frank W. Horner Ltd., Town of Mount Royal, Quebec.

TABLE I

The chemical shifts (τ) of some protons in compounds **2–8**

| Compound | $J_{4,7}$(Hz)* at 150° (DMSO-$d_6$) | DMSO-$d_6$ | | | $CF_3COOH$ | | | $CDCl_3$ | | | $D_2O$† | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | P-H‡ | $C_4$-H | $C_7$-H | P-H‡ | $C_4$-H | $C_7$-H | P-H‡ | $C_4$-H | $C_7$-H | P-H‡ | $C_4$-H | $C_7$-H |
| **2** | 2.5 | 7.30 | 6.73 | 5.67 | 6.95 | 6.03 | 5.08 | — | — | — | — | — | — |
| **3** | 3.0 | 7.45 | 6.82 | 5.74 | — | — | — | — | — | — | — | — | — |
| **4**§ | 3.0 | 7.30 | 6.70 | 5.68 | 6.90 | 6.02 | 4.97 | — | — | — | 7.40 | 6.76 | 5.86 |
| **5**‖ | 3.0 | 7.50 | 6.80 | 5.70 | 6.89 | 6.00 | 4.87 | — | — | — | 7.60 | 6.92 | 5.93 |
| **6** | 3.0 | 7.46 | 6.90 | 5.82 | — | — | — | 7.32 | 6.70 | 5.66 | — | — | — |
| **7** | 3.0 | 7.50 | 6.87 | 5.80 | — | — | — | — | — | — | — | — | — |
| **8** | 3.0 | 7.58 | 6.90 | 5.80 | — | — | — | 7.46 | 6.76 | 5.70 | — | — | — |

*All signals were triplets.
†The chemical shift of the HOD signal (assigned 5.30) was used as an internal standard.
‡Protons on the propionic methylenes.
§Potassium salt in $D_2O$.
‖Sodium salt in $D_2O$.

The nuclear magnetic resonance (n.m.r.) spectra of the lactams **2–8** suggested homoallylic coupling between the $C_4$- and $C_7$-protons. These appear as broad singlets, $w_{1/2}$ = 7–9 Hz at 35°, and as well-resolved triplets, $J_{4,7}$ = 2.5–3.0 Hz at 150° (Table I). Analogous homoallylic coupling had been noted (4,5), particularly in **11** (6) which had $J_{2,5}$ = 3.0 Hz. In contrast to these signals for the $C_4$- and $C_7$-protons in **4** and **5**, those for the corresponding protons in the open forms **9** (K salt in $D_2O$: $C_4$- and $C_7$-protons at τ 6.63 and τ 5.90) and **10** (Na salt in $D_2O$: $C_4$- and $C_7$-protons at τ 6.80 and τ 6.49) were all sharp singlets indicating no homoallylic coupling.

After the lactam **2** had stood for one week in DMSO-$d_6$/KOBu$^t$ at 50°, its spectrum at 150° showed no $C_4$-proton signal at τ 6.73 and the triplet at τ 5.67 for the $C_7$-protons had collapsed to a singlet. As this could only be ascribed to deuteration at $C_4$, it established both the assignments for the $C_4$- and $C_7$-protons and also the homoallylic coupling. Again the open analogues **9** and **10** differed, showing no exchange in alkaline $D_2O$.

In 2 *N* KOD/$D_2O$, **4** was rapidly deuterated at $C_4$ and more slowly hydrolyzed to largely $C_4$-deuterated **9**. Here the $C_4$-proton signal at τ 6.90 was largely eliminated in 7 min, completely in 1 h, and the appearance of a small sharp singlet at τ 6.75 indicated some hydrolysis to **9** prior to the deuteration. Concurrently, the $C_7$-proton signal of **4** at τ 6.02 first sharpened, then was replaced by the sharp singlet at τ 6.52 representing $C_7$-protons of **9**, whether or not deuterated at $C_4$. At the same time, the signal for the propionic methylenes of **4**, a poorly-resolved multiplet at τ 7.57, became a well-resolved multiplet at τ 7.45, identical with that observed in the spectrum of the potassium salt of **9**. The spectrum of the recovered deuterated **9** in $CF_3COOH$ was identical with that of **9** except that the 2H singlet at τ 6.02 ($C_4$-protons) had almost disappeared. Here the $C_7$-protons of **9** appear as a quartet (τ 5.33, *J* = 5.5 Hz) in $CF_3COOH$ but as a singlet in $CF_3COOD$; evidently the quartet arises from coupling of the $C_7$-protons with those of the protonated amino group.

In 1 *N* NaOD/$D_2O$, **5** behaved analogously. Within 15 min it was deuterated on $C_4$ then converted into $C_4$-deuterated **10**, a little undeuterated **10** being formed also.

The same homoallylic coupling and deuterium exchange was found in the less closely related lactam **12**, which was prepared for the purpose. Its n.m.r. spectrum in $CDCl_3$ showed the $C_4$-protons as a poorly resolved triplet (τ 6.47, *J* = 1.5 Hz) and the $C_1$-protons as a broad singlet (τ 5.57, $w_{1/2}$ = 5.0 Hz). The spectrum in DMSO-$d_6$ at 130° was no better resolved. After **12** was deuterated by leaving it in $CH_3ONa/CH_3OD$ for 3 days at 20°, its spectrum showed no signal at τ 6.47 and that at τ 5.57 was sharper ($w_{1/2}$ = 3.3 Hz).

## Experimental

Compounds **2,4,5** and **10** (2), **3** (3) and **6–8** (1) were obtained by literature methods.

### *1,4-Dihydro-3[2H]-isoquinolone (12)*

In a 250 ml flask fitted with a magnetic stirrer, condenser and drying tube, were placed 150 ml of THF and 1 g of 2-thiohomophthalimide (7). Two teaspoons of Raney Nickel (Grace No. 28) were added as a slurry in 50 ml of THF and the mixture was stirred and refluxed for 3 h. The nickel was filtered off within an hour for, if the mixture first stood overnight, an unidentified compound m.p. 300° containing nickel was the only product obtained. The filtrate was evaporated and the residue was crystallized from aqueous acetone (Darco) as greenish-yellow crystals (0.54 g, 65%), m.p. 150–152° (lit. (8): colorless crystals, m.p. 149.5–150.5°); infrared spectrum (Nujol): 3330 $\mathrm{cm^{-1}}$, 3200 $\mathrm{cm^{-1}}$ ($\nu_{NH}$), 3050 $\mathrm{cm^{-1}}$ ($\nu_{CH}$ aromatic), 1665 $\mathrm{cm^{-1}}$ ($\nu_{CO}$ amide), 1606 $\mathrm{cm^{-1}}$ ($\nu_{C:C}$), 748 $\mathrm{cm^{-1}}$ ($\delta_{CH}$ aromatic); n.m.r. spectrum ($CDCl_3$): $\tau$ 6.47 ($C_4$-H) (on expanding the spectrum, this signal became a poorly-resolved triplet, $J$ = 1.5 Hz), $\tau$ 5.57 (s, $C_1$-H), $\tau$ 2.89 (aromatic), $\tau$ 2.00 (NH); mass spectrum, $m/e$ = 147 (mol. wt., 147.18).

Anal. Calcd. for $C_9H_9NO$: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.53; H, 5.98; N, 9.34.

## Acknowledgment

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# Reissert compound studies. XXI. Arylation reactions[1]

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The anions derived from both the isoquinoline and the quinoline Reissert compounds have been arylated by use of nitro and dinitro arylhalides. *p*-Fluorobenzaldehyde reacts preferentially at the carbonyl group and does not lead to arylation.

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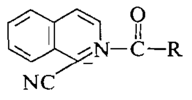
A variety of reactions have been reported for the anions **1** and **2** derived from the isoquinoline and quinoline Reissert compounds (2). We now wish to report on the arylation of these anions.



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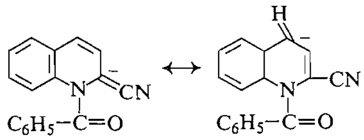
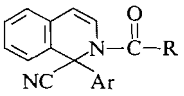


**2**

Reaction of the anion **1** (R = $CH_3$ or $C_6H_5$) derived from the appropriate isoquinoline Reissert compound and sodium hydride in dimethylformamide (3) with 2,4-dinitrofluorobenzene gave **3** (R = $CH_3$ or $C_6H_5$; Ar = 2,4-$(NO_2)_2C_6H_3$) which could be hydrolyzed to **4** (Ar = 2,4-$(NO_2)_2C_6H_3$). Reaction of **1** (R = $CH_3$ or $C_6H_5$) under the same conditions with 2-bromo-3-nitropyridine proceeded in a similar manner to give **3** (R = $CH_3$ or $C_6H_5$; Ar = 2-(3-$NO_2C_5H_3N$)) which could be hydrolyzed to 1-(3-nitro-2-pyridyl) isoquinoline (**4**, Ar = 2-(3-$NO_2C_5H_3N$)). For unexplained reasons the



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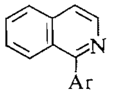

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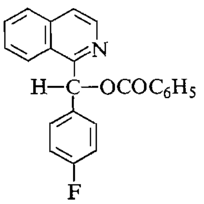

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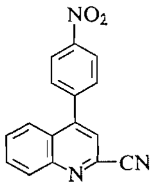

**6**

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[1] For Part XX, see Reference 1.
[2] N.S.F. Undergraduate Research Participant.