

Stanley Wawzonek\* and Thien Van Truong

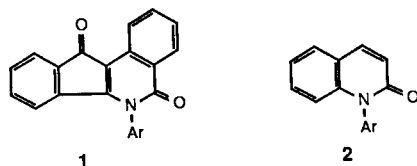
Department of Chemistry, The University of Iowa,  
Iowa City, Iowa 52242  
Received July 16, 1987

Dedicated to Professor Norman H. Cromwell

1-Phenyl-, 1-*m*-tolyl- and 1-*p*-tolyl-1,2-dihydro-2-quinolone have been prepared by treating the potassium derivative of 1,2-dihydro-2-quinolone with the corresponding aryl bromide in the presence of finely divided copper. The use of *o*-bromotoluene in this reaction gave trace amounts of a crystalline material which upon the basis of mass spectrum analysis was assigned 2-*o*-tolylxyquinoline as a structure. The 1-aryl groups caused an unusual chemical shift of the 8-proton to the  $\delta$  6.64-6.70 region. This behavior paralleled that observed for the 7-proton of 6-phenyl-6*H*-indeno[1,2-*c*]isoquinoline-5,11-dione in earlier studies.

*J. Heterocyclic Chem.*, **25**, 381 (1988).

In a study of the synthesis of 6-substituted-6*H*-indeno[1,2-*c*]isoquinoline-5,11-diones **1** for testing as anti-tumor agents [1] in The National Cancer Institute 3P S31 Test



the 6-phenyl- (R = C<sub>6</sub>H<sub>5</sub>, **1**) and 6-[3-pyridyl]- (R = 3-C<sub>5</sub>H<sub>4</sub>, **1**) derivatives showed unusual chemical shifts in their nmr spectra for the 7-proton which was ascribed to shielding by the 6-aryl group. This assignment was based solely on the arrangement of the aryl groups in models of these compounds.

To confirm this assignment the simple analogs, 1-aryl-1,2-dihydro-2-quinolones **2** were prepared by treating the potassium derivative of 1,2-dihydro-2-quinolone with bromobenzene, *p*-bromotoluene and *m*-bromotoluene in the presence of finely divided copper at 250° using the directions given for the preparation of the 1-phenyl derivative [2].

This reaction failed for the preparation of the 1-*o*-tolyl derivative **2** (Ar = *o*-C<sub>7</sub>H<sub>7</sub>); trace amounts of a crystalline material were obtained which was volatile with steam. Mass spectrum analysis suggested 2-*o*-tolylxyquinoline as a structure since it was different from that observed with the *p*- and *m*-derivatives **2** (Ar = *p*- and *m*-C<sub>7</sub>H<sub>7</sub>) and resembled the mass spectrum of the 1-phenyl derivative with respect to the base peaks.

The chemical shifts observed for the 3,4,8-protons of 1,2-dihydro-2-quinolone and the 1-aryl derivatives **2** are given in Table I. All the protons listed appear as doublets except the 8-proton in the unsubstituted quinoline; the expected doublet overlaps with a triplet for either the 6- or 7-proton and appears in a multiplet at  $\delta$  7.47-7.53.

Table I

Chemical Shifts for Selective Protons in 1,2-Dihydro-2-quinolone and Its 1-Aryl Derivatives **2**

1,2-Dihydro-2-quinolones	Chemical Shifts ( $\delta$ )		
	3-H [a]	4-H [a]	8-H [b]
Unsubstituted	6.73	7.82	7.47-7.53
1-Phenyl	6.78	7.75	6.64
1- <i>p</i> -Tolyl	6.83	7.82	6.70
1- <i>m</i> -Tolyl	6.78	7.77	6.66

[a] J = 9.5-9.6 Hz. [b] J = 8.4 Hz.

Temperature variation from -30° to 70° had no effect on the chemical shift of the 8-proton but shifted the values for the 3- and 4-hydrogens from  $\delta$  6.84 and 7.84 at -30°, respectively to  $\delta$  6.70 and 7.70 at 70°. Similar shifts were

Table II

Temperature Effects on the Chemical Shifts of 3-, 4-, and 8-Protons in 1-Phenyl-1,2-dihydro-2-quinolone **2** (Ar = C<sub>6</sub>H<sub>5</sub>)

Temperature C	3-H	4-H	8-H
-30°	6.84	7.84	6.63
0°	5.78	7.78	6.63
25°	6.75	7.74	6.64
70°	6.70	7.70	6.62

observed for these hydrogens in the *p*-tolyl derivative and in coumarin; the latter showed a change in chemical shifts from  $\delta$  6.39 and 7.72 at 25° to 6.45 and 7.79 at -33° respectively. The reason for this temperature effect is not apparent at the present time.

The chemical shifts for the <sup>13</sup>C nmr spectra of the 3- and 4-carbons in the *p*-tolyl derivative **2** (Ar = *p*-C<sub>7</sub>H<sub>7</sub>) showed only minor changes with temperature changes of -25° to +25°; the values at -25° were 115.91 and 139.76, respectively and at +25° were 115.96 and 139.60.

The shift of the 8-proton in the 1-aryl derivatives **2** to

the  $\delta = 6.64$ - $6.70$  region suggested that the proton is shielded by the 1-aryl group, **2**. Since stereochemical assignments by nmr spectra are not always infallible [3,4], a crystal structure of the 1-phenyl derivative was carried out and indicated that the 1-aryl ring is rotated to make a dihedral angle of  $71.8^\circ$  with the quinolone ring [5]. This arrangement orients the ring electrons in a manner which would account for the abnormal chemical shifts observed. Rotation of the aryl group by increasing the temperature has no effect on this interaction.

#### EXPERIMENTAL

Melting points are uncorrected. The ir spectra were determined with a Perkin-Elmer Model 137B spectrophotometer. The nmr spectra were obtained with a 360 MHz Bruker spectrometer. Mass spectra were measured with a Hewlett-Packard Model 5985 AGC-M5 system.

##### 1,2-Dihydro-2-quinolone.

This compound was prepared by the oxidation of quinoline by hypochlorous acid [6];  $^1\text{H}$  nmr (deuteriochloroform):  $\delta$  6.73 (d, 1H, 3-H,  $J = 9.5$  Hz), 7.21 (t, 1H, 7-H,  $J = 8.1$  Hz), 7.47-7.53 (m, 2-H, 6-, 8-Hs), 7.56 (d, 1-H, 5-H,  $J = 7.8$  Hz), 7.82 (d, 1H, 4-H,  $J = 9.5$  Hz), 12.72 (broad singlet, 1H, N-H).

##### 1-Phenyl-1,2-dihydro-2-quinolone **2** (Ar = $\text{C}_6\text{H}_5$ ).

This compound was prepared by treating the potassium derivative of 1,2-dihydro-2-quinolone with bromobenzene in the presence of finely divided copper at  $250^\circ$  [2];  $^1\text{H}$  nmr (deuteriochloroform):  $\delta$  6.64 (d, 1H, 8-H,  $J = 8.4$  Hz), 6.78 (d, 1H, 3-H,  $J = 9.5$  Hz), 7.18 (t, 1H, 7-H,  $J = 7.5$  Hz), 7.25-7.34 (m, 3H, 6-, 2', 6'-Hs), 7.52 (d, 1H, 5-H,  $J = 7.3$  Hz), 7.59 (t, 3H, 3', 4', 5'-Hs,  $J = 7.8$  Hz), 7.75 (d, 1H, 4-H,  $J = 9.5$  Hz); ms: m/e (%) 229 (9.9,  $\text{M}^+ + 1$ ), 221 (61.6, M), 220 (100,  $\text{M}^+ - 1$ ).

##### 1-*p*-Tolyl-1,2-dihydro-2-quinolone **2** (Ar = *p*- $\text{C}_6\text{H}_7$ ).

This compound was prepared in a 19% yield using the procedure given for the 1-phenyl derivative. Recrystallization from petroleum ether

(bp  $60$ - $68^\circ$ ) after chromatography on silica and on alumina gave a sample melting at  $152$ - $154^\circ$ ; ir (Nujol):  $6.06 \mu$  (C=O);  $^1\text{H}$  nmr (deuteriochloroform):  $\delta$  2.45 (s, 3H,  $\text{CH}_3$ ), 6.68 (d, 1H, 8-H,  $J = 8.5$  Hz), 6.76 (d, 1H, 3-H,  $J = 9.5$  Hz), 7.15 (d, 2H, 3', 5'-Hs,  $J = 8.3$  Hz), 7.24 (t, 1H, 7-H,  $J = 8.2$  Hz), 7.31 (t, 1H, 6-H,  $J = 8.2$  Hz), 7.38 (d, 2H, 2', 6'-Hs,  $J = 8.2$  Hz), 7.56 (d, 1H, 5-H,  $J = 7.7$  Hz), 7.76 (d, 1H, 4-H,  $J = 9.6$  Hz); ms: m/e (%) 236 (9.3,  $\text{M}^+ + 1$ ), 235 (57.7,  $\text{M}^+$ ), 234 (100,  $\text{M}^+ - 1$ ).

*Anal.* Calcd. for  $\text{C}_{16}\text{H}_{13}\text{NO}$ : C, 81.70; H, 5.54; N, 5.96. Found: C, 81.72; H, 5.59; N, 5.83.

##### 1-*m*-Tolyl-1,2-dihydro-2-quinolone **2** (Ar = *m*- $\text{C}_6\text{H}_7$ ).

This compound was prepared in a 6% yield using the procedure given for the 1-phenyl derivative. Recrystallization from petroleum ether (bp  $60$ - $68^\circ$ ) gave a sample melting at  $99$ - $100.5^\circ$ ; ir (Nujol):  $6.02 \mu$  (C=O);  $^1\text{H}$  nmr (deuteriochloroform):  $\delta$  2.43 (s, 3H,  $\text{CH}_3$ ), 6.66 (d, 1H, 8-H,  $J = 8.4$  Hz), 6.77 (d, 1H, 3-H,  $J = 9.6$  Hz), 7.07 (d, 1H, 6'-H,  $J = 8.3$  Hz), 7.09 (s, 1H, 2'-H), 7.18 (t, 1H, 7-H,  $J = 7.4$  Hz), 7.30-7.34 (m, 2H, 6-, 5'-Hs), 7.4 (t, 1H, 4'-H,  $J = 7.6$  Hz), 7.57 (d, 1H, 5-H,  $J = 7.8$  Hz), 7.77 (d, 1H, 4-H,  $J = 9.6$  Hz); ms: m/e (%) 236 (9.4,  $\text{M}^+ + 1$ ), 235 (58,  $\text{M}^+$ ), 234 (100,  $\text{M}^+ - 1$ ).

*Anal.* Calcd. for  $\text{C}_{16}\text{H}_{13}\text{NO}$ : C, 81.70; H, 5.54; N, 5.96. Found: C, 81.99; H, 5.33; N, 5.55.

##### 2-*o*-Tolyloxyquinoline.

Attempts to prepare the 1-*o*-tolyl derivative **2** (Ar = *o*- $\text{C}_6\text{H}_7$ ) gave a trace amount of a crystalline material which was volatile with steam. The amount was only sufficient for a mass spectrum analysis: m/e (%) 236 (10.2,  $\text{M}^+ + 1$ ), 235 (57.1,  $\text{M}^+$ ), 234 (33.9,  $\text{M}^+ - 1$ ), 221 (6.3,  $\text{M}^+ + 1 - \text{CH}_3$ ), 220 (35.6,  $\text{M}^+ - \text{CH}_3$ ), 219 (18.9,  $\text{M}^+ - 1 - \text{CH}_3$ ), 218 (100,  $-2 - \text{CH}_3$ ).

#### REFERENCES AND NOTES

- [1] S. Wawzonek, *Org. Prepn. Proced. Int.*, **14**, 163 (1982).
- [2] A. E. Tschitschibabin and N. P. Jeletsky, *Ber.*, **57**, 1158 (1924).
- [3] N. C. Baenziger, S. Wawzonek and D. C. Swenson, *Acta Cryst.*, **B35**, 2793 (1979).
- [4] S. Wawzonek, E. Smolin and J. E. Durham, *Org. Magn. Reson.*, **6**, 547 (1974).
- [5] N. C. Baenziger and S. Wawzonek, *Acta Cryst.*, **C40**, 1576 (1984).
- [6] A. Einhorn and R. Lauch, *Chem. Ber.*, **19**, 53 (1956).