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# An Unusual Formation of A Novel Spiroisoquinolone ring

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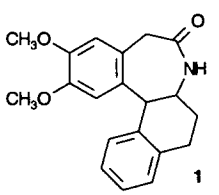
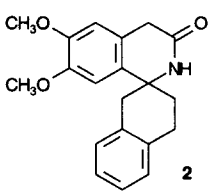
***Abstract:*** *A new spiro[napthalene-2(1H)-1'(2'H)-isoquinol-3-one] 2 was obtained after treatment of amidoalcohol 4 with polyphosphoric acid.*

Spirocyclic compounds demonstrate diverse biological properties ranging from central nervous system activity to anti-tumor and anti-fungal effects.[1] This report describes the synthesis of a novel spiroisoquinolone.

In an effort to synthesize benzo[d]naptho[2,1-b]benzazepinone **1**, spiro compound **2** was obtained. The synthetic strategy is illustrated in Scheme 1. The aminoalcohol **3** was prepared following a known procedure starting from 2-bromo-1-tetralone.[2] Reaction of **3** with 3,4-dimethoxyphenylacetyl chloride in the presence of triethylamine gave amidoalcohol **4.** Since carbocations are more stable at a benzylic position it was anticipated that on acid cyclization **4** would give **1**. Treatment with neat methanesulfonic acid at temperatures from 0 °C to 23 °C, yielded the dehydrated compound **5**. To our surprise, however, treatment of **4** with polyphosphoric acid (PPA) at 100 °C for 90 min gave **2** as a crystalline solid. The structure of the compound was confirmed by spectroscopic analysis to be 6',7'-dimethoxy-3'-oxo-3,3',4,4'-tetrahydrospiro[napthalene-2(1*H*), 1'(2'*H*)-isoquinoline] (**2**).



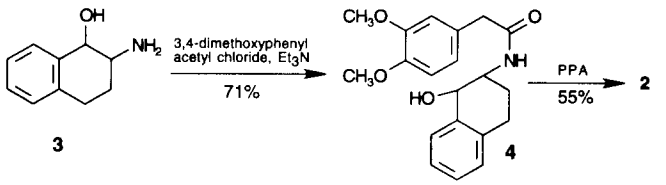

**1**



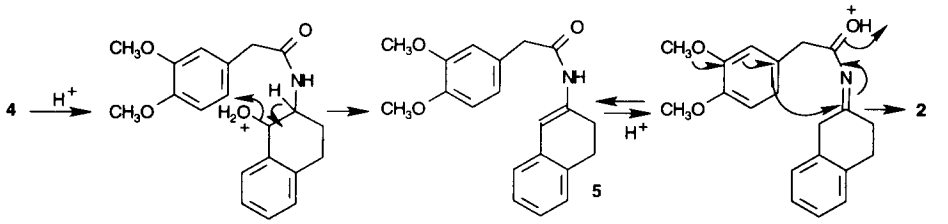

**2**

A possible mechanism for formation of this spirocyclic compound is illustrated in Scheme 2. Protonation of **4** followed by dehydration leads to **5**. The tautomeric iminium form of **5** then undergoes attack by the activated aromatic ring to form the spirocyclic **2**. In order to test this hypothesis, enamide **5** was subjected to the same cyclization conditions (PPA, 100 °C). After a similar work-up, **2** was isolated as the only product. All the spectral and analytical data were in agreement with the proposed chemical structures.[3]

**Scheme 1**




**Scheme 2**




**Acknowledgments:**

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**References and Notes:**

1. (a) Bauer, V. J.; Duffy, B. J.; Hoffman, D.; Klioze, S. S.; Kosley, R. W. Jr.; McFadden, A.R.; Martin, L. L.; Ong, H. H. *J. Med. Chem.* **1976**, *19*, 1315. (b) Fish, P.V.; Pattenden G. *Tetrahedron Lett.* **1988**, *29*, 3857. (c) Yamato, M.; Takeuchi, Y.; Tomozane, H. *Synthesis* **1990**, *7*, 569.

2. (a) Riggs, R. M. Ph.D. Thesis, Purdue University, 1986. (b) Bowman, R.; Evans, D.; Guyett, J.; Nagy, H.; Weak, J.; Weyell, D. *J. Chem. Soc. Perkin I.* **1973**, 438.

3. Analytical and Spectral Data:

**2**: mp 224-226 °C; $^1$H NMR ($CDCl_3$, 500 MHz) δ 2.06 (m, 1H), 2.18 (m, 1H), 2.76 (d, *J* = 17 Hz, 1H), 3.00 (m, 2H), 3.48 (d, *J* = 16 Hz, 1H), 3.60 (d, *J* = 20 Hz, 1H, CHCO), 3.68 (d, *J* = 20 Hz, 1H, CHCO), 3. 79 (s, 3H, $OCH_3$), 3.90 (s, 3H, $OCH_3$), 6. 17 (broad s, 1H, NH), 6.66 (s, 1H, ArH), 6.75 (s, 1H, ArH), 7. 16 (m, 4H, ArH); $^{13}$C-APT ($CDCl_3$, 125.697 MHz) δ 26.10, 35.88, 35.95, 42.41 and 56.99 (aliphatic, all up); 107.32, 110.66, 126.60, 126.89, 129.05, 129.78 (aromatics, all up); 56.05 and 56.06 ($OCH_3$, down); 123.15, 130.50, 132.89, 134.17, 132.89, 134.17, 147.17, 147.97 and 148.53 (aromatics, all down), 170.59 (C=O); [quarternary and $CH_2$ are up; methyl and CH are down]; CIMS m/e 324 (M+1); Anal. for $C_{20}H_{21}NO_3$ (within ± 4%).

**3:** mp (HCl) 188-189 °C (mixture of cis & trans); $^1$H NMR($CDCl_3$) δ 4.32 (d, *J* = 6.7 Hz, 1H, CH-trans), 4.52 (d, *J* = 3.9 Hz, 1H, CH-cis); *Chem. Abstr.* **1921**, *15*, 2093.

**4**: mp 169-171 °C; $^1$HNMR ($CDCl_3$) δ 3.54 (s, 2H, $CH_2CO$); Anal. $C_{20}H_{23}NO_4$ (± 4%).

**5**: mp 156-158 °C; $^1$HNMR ($CDCl_3$) δ 3.52 (d, *J* = 15 Hz, 1H, CHCO), 3.58 (d, *J* = 15 Hz, 1H, CHCO); HRMS calcd for $C_{20}H_{21}NO_3$ 324.1600, found 324.1610.

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