Differences of pH-Dependent Mechanisms on Generation of Hydride Donors using Ru(II) Complexes Containing Geometric Isomers of NAD^+ Model Ligands: NMR and Radiolysis Studies in Aqueous Solution

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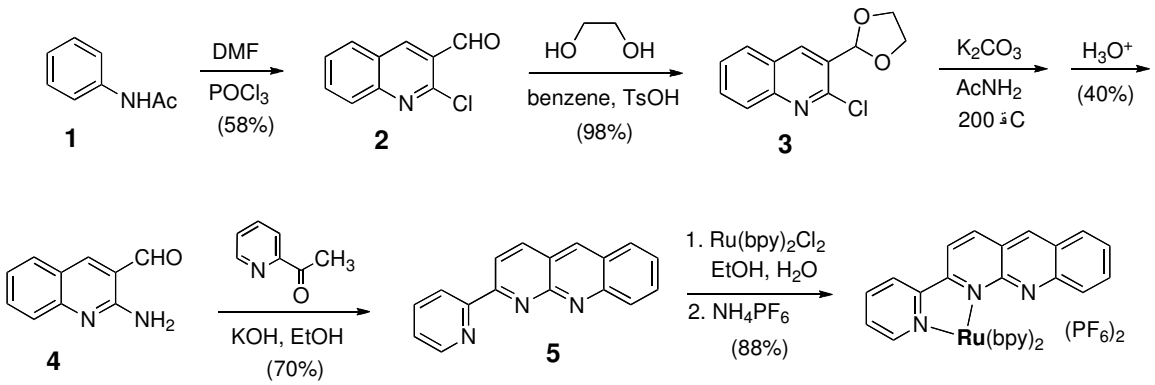
Supporting Information

Synthesis and Characterization

The 2-aminoquinoline-3-carbaldehyde (**4**) was prepared in four steps starting from acetanilide (Scheme S1). Following the Meth-Cohn quinoline synthesis under Vilsmeier-Haack formylation conditions, acetanilide was transformed into 2-chloroquinoline-3-carbaldehyde (**2**) in moderate yield.[1] Direct amination of this species with ammonia[2] was unsuccessful and therefore the chlorocarbaldehyde **2** was protected with ethylene glycol to give the acetal **3**.[3,4] The reaction of **3** and acetamide in the presence of K_2CO_3 at 200 $^{\circ}$C,[3,5] followed by deprotection under acidic conditions, afforded the *o*-aminocarbaldehyde **4** in 17-40% yield. The amino-aldehyde is characterized by its ^{1}H and ^{13}C NMR spectra. Seven proton signals including a singlet at 10.05 ppm for the aldehyde and a broad peak at 6.61 ppm for the amino group, as well as ten ^{13}C peaks, match well to the expected structure. The Friedländer condensation of **4** and 2-acetylpyridine was straightforward[6] and the resulting ligand was characterized by its proton and ^{13}C NMR spectra. When **5** was treated with $[Ru(bpy)_2Cl_2]$ in aqueous ethanol, followed by counterion exchange with NH_4PF_6, the complex $[Ru(bpy)_2(\mathbf{5})](PF_6)_2$ was obtained in 88% yield. This complex showed mass spectrum peaks at m/z = 816.12 and 671.20 corresponding to $[Ru(bpy)_2(\mathbf{5})(PF_6)]^+$ and $[Ru(bpy)_2(\mathbf{5})]^+$. Every proton in the complex is magnetically non-equivalent, leading to 27 signals in its ^{1}H NMR. To simplify the spectrum and better characterize the complex as well as its reaction products, the dueuterio analogue $[Ru(bpy\text{-}d_8)_2(\mathbf{5})](PF_6)_2$ was prepared in a similar fashion. This dueterio complex exhibits only ^{1}H NMR signals of ligand **5**, which could be assigned by an ^{1}H-^{1}H COSY spectrum.

Scheme S1. Synthesis of 3-(pyrid-2'-yl)-4-azaacridine and its Ru(II) complex.



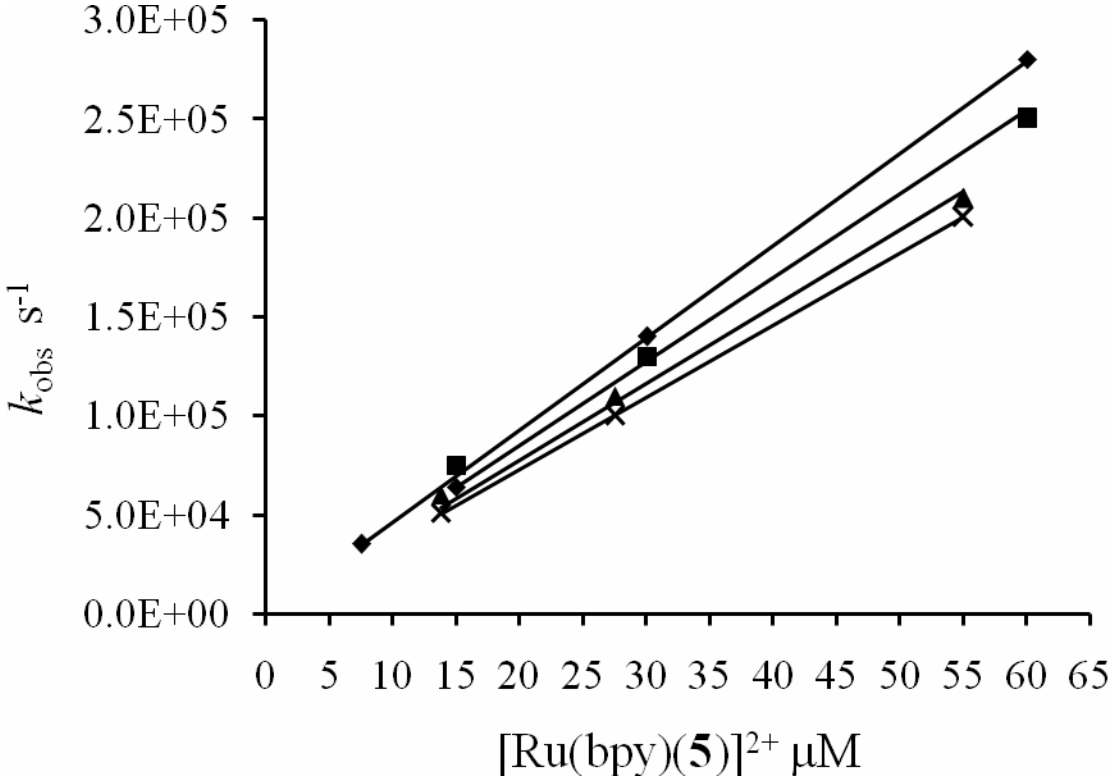


Figure S1. Concentration dependence between $CO_2^{\bullet-}$ and $[Ru(bpy)_2(\mathbf{5})]^{2+}$ at pH 7.3 and 12.5 in H_2O and D_2O (diamond: pH 12.5, H_2O, square: pH 7.3, H_2O, triangle: pH 12.6, D_2O, cross: pH 7.3, D_2O).

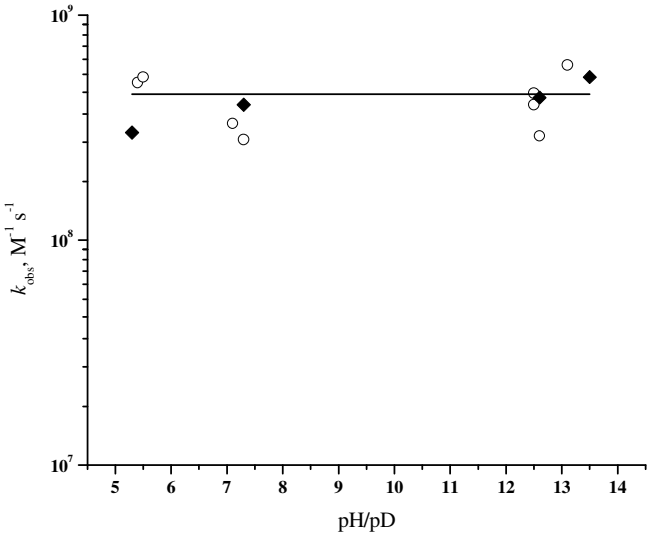


Figure S2. The pH-dependence of the observed second-order rate constants for the disappearance of $[Ru(bpy)_2(\mathbf{5}^{\bullet-})]^+$ and $[Ru(bpy)_2(\mathbf{5}H^{\bullet})]^{2+}$ (in H_2O = circles; in D_2O = diamonds).

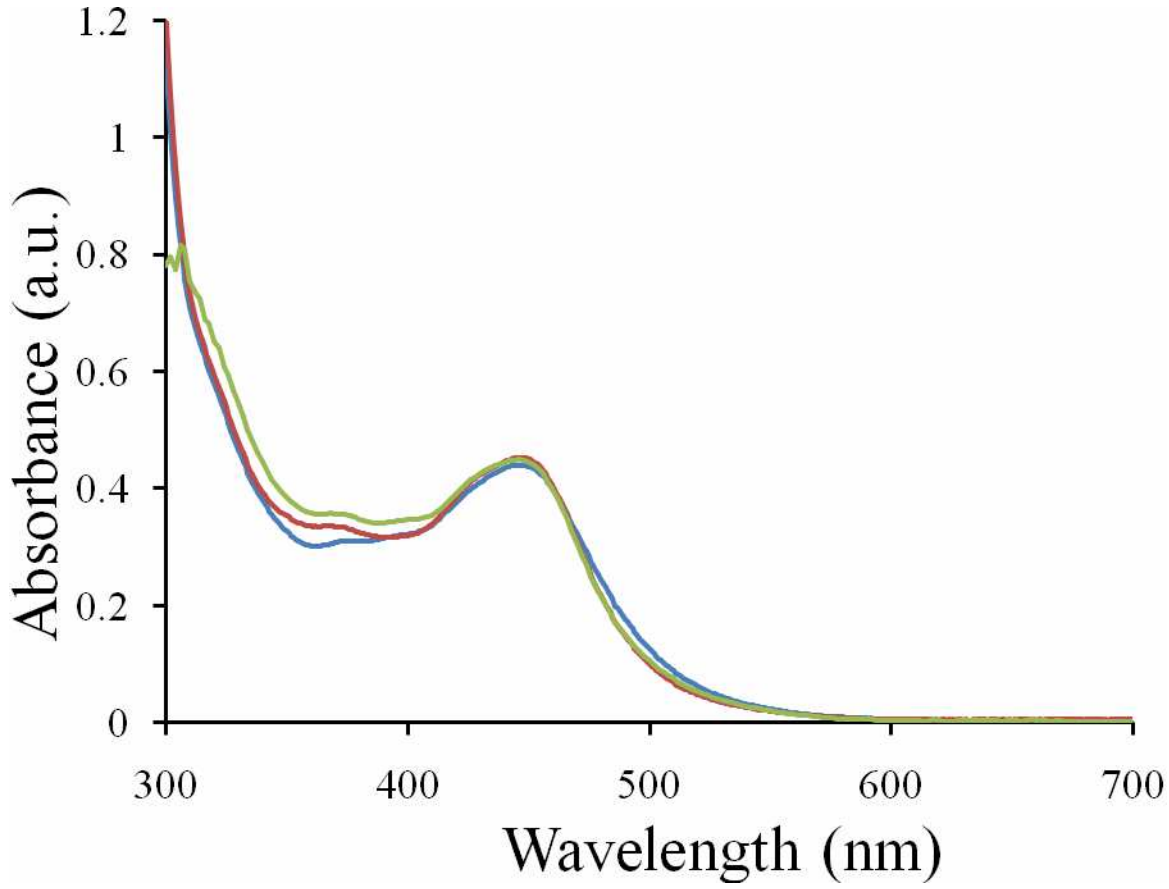


Figure S3. UV-vis comparison of $[Ru(bpy)_2(\mathbf{5}HH)]^{2+}$ (green), final spectra made at pH = 9.1 during ^{60}Co experiment (red) and chemically made $[(Ru(bpy)_2(\mathbf{5})]_2^{4+}$ (blue).

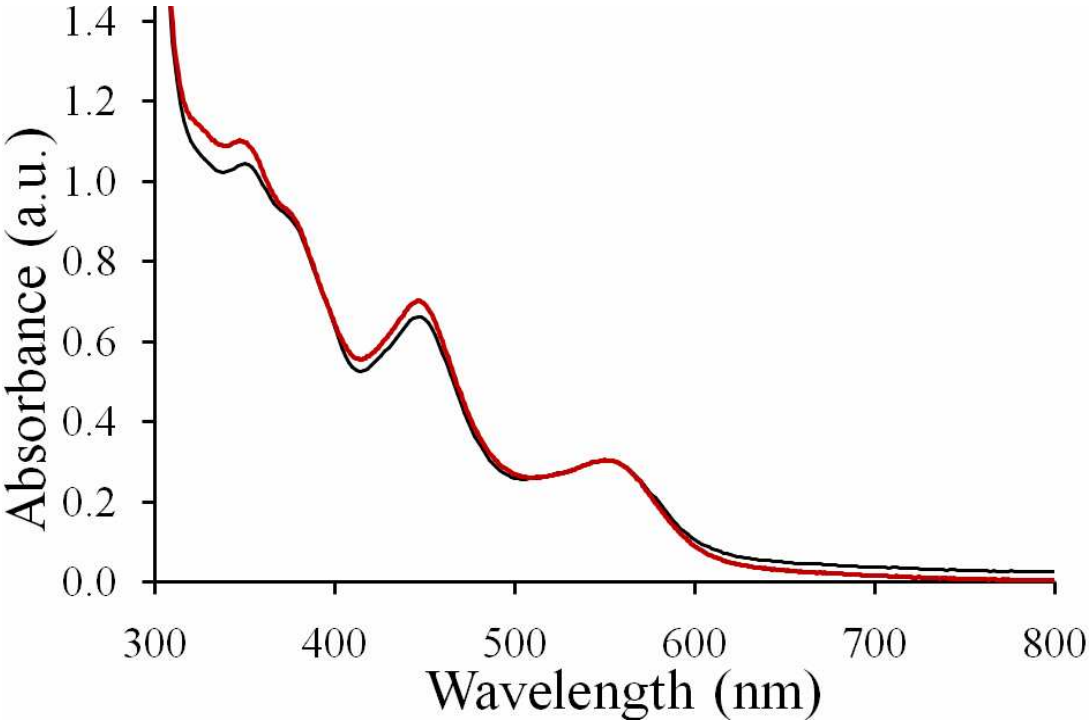


Figure S4. UV-vis comparison of sum of ½ $[(Ru(bpy)_2(\mathbf{5})]^{2+}$ and ½ $[Ru(bpy)_2(\mathbf{5}HH)]^{2+}$ (black) with that of product after 100 seconds (^{60}Co experiment) at pH 13.3 (red).

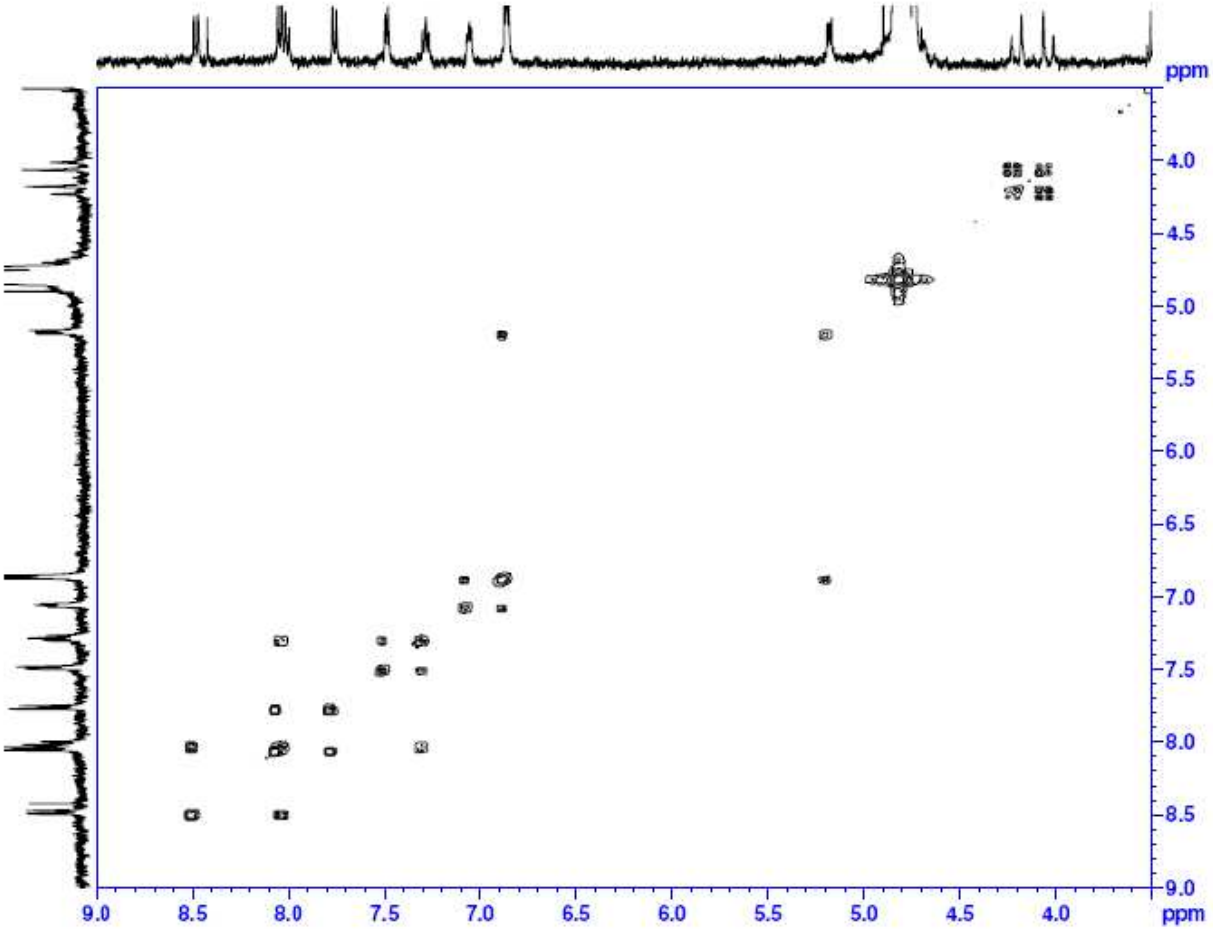


Figure S5. 2D gradient COSY of $[Ru(bpy)_2(\mathbf{5}HH)]^{2+}$ made chemically in D_2O/CD_3OD.

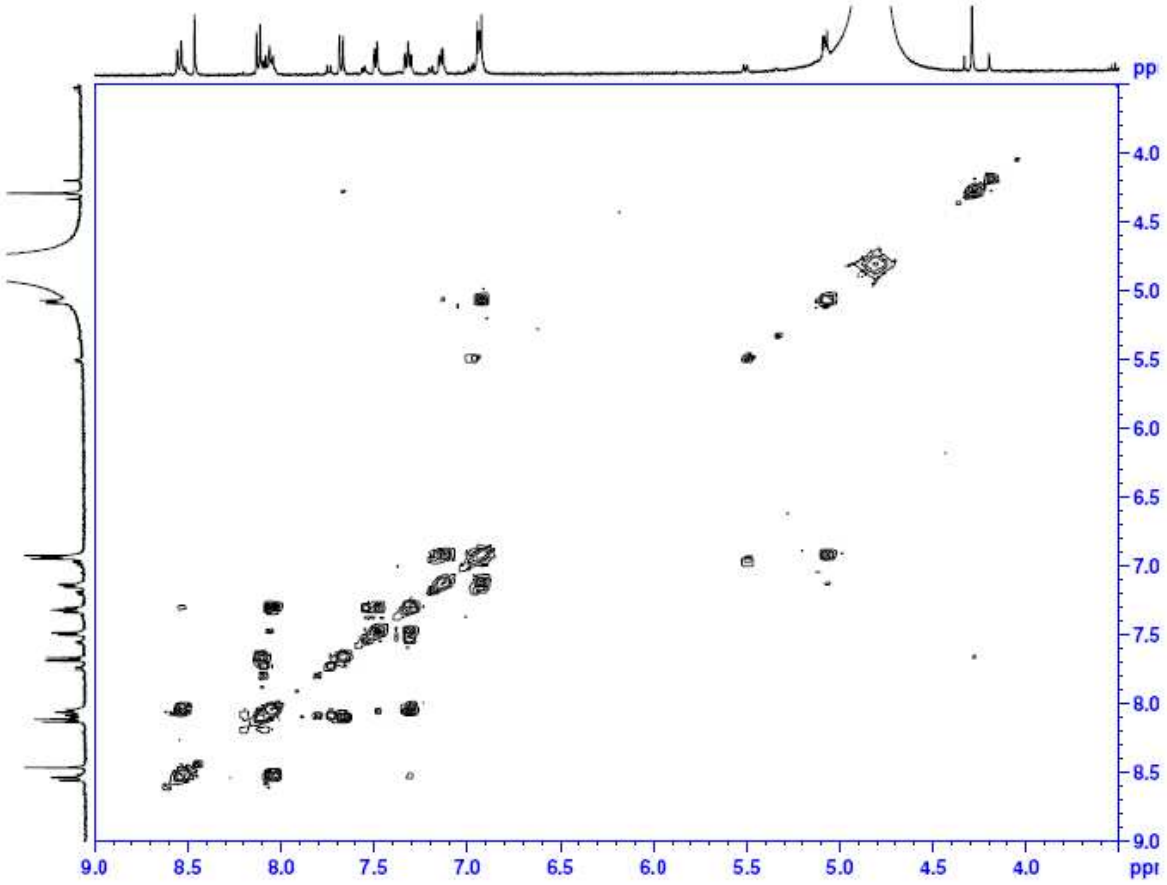


Figure S6. 2D gradient COSY of $[(Ru(bpy)_2(\mathbf{5}H)]_2^{4+}$ in D_2O/CD_3OD.

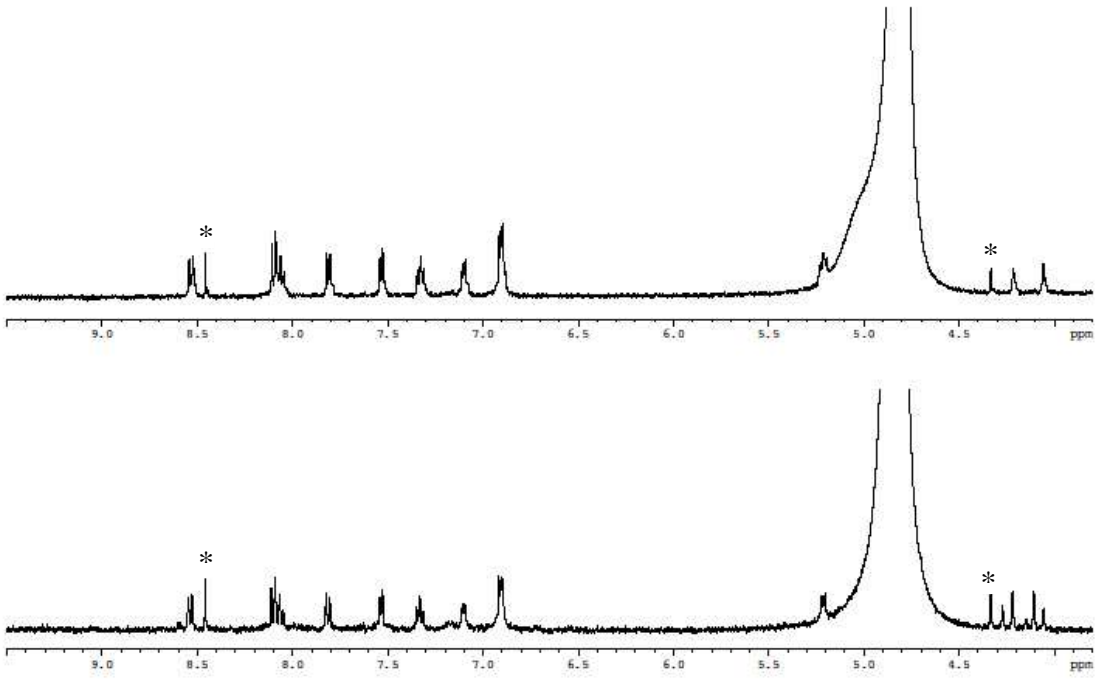


Figure S7. ^{1}H NMR in D_2O/CD_3OD of photochemical decomposition of $[Ru(bpy\text{-}d_8)_2(\mathbf{5}H)]_2^{4+}$ photolyzed in H_2O/MeOH (bottom) or D_2O/CD_3OD (top) with excess Na_2SO_4 present. Impurities labeled (*).

References

(1) Meth-Cohn, O.; Narine, B.; Tarnowski, B. *Tetrahedron Lett.* **1979**, *20*, 3111.

(2) Meth-Cohn, O.; Narine, B.; Tarnowski, B. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1520.

(3) Nyerges, M.; Pinter, A.; Viranyi, A.; Blasko, G.; Toke, L. *Tetrahedron* **2005**, *61*, 8199.

(4) Farghaly, A. M.; Habib, N. S.; Khalil, M. A.; El-Sayed, O. A.; Bistawroos, A. E. *Archiv der Pharmazie* **1990**, *323*, 247.

(5) Inglis, S.; Jones, R.; Fritz, D.; Stojkoski, C.; Booker, G.; Pyke, S. *Org. Biomol. Chem.* **2005**, *3*, 2543.

(6) Godard, A.; Queguiner, G. *J. Heterocycl. Chem.* **1982**, *19*, 1289.