Pergamon

Tetrahedron Letters 41 (2000) 4039–4042

TETRAHEDRON
LETTERS

Synthesis of derivatized amino acids for the study of electron transfer

Scafford A. Serron, W. Stephen Aldridge III, Ryan M. Danell and Thomas J. Meyer *,†

Department of Chemistry, University of North Carolina at Chapel Hill, CB # 3290, Chapel Hill, NC 27599-3290, USA

Received 10 February 2000; revised 3 April 2000; accepted 5 April 2000

Abstract

The synthesis of a new electron transfer donor and two new ruthenium chromophores are described based on coupling to derivatized proline residues for the purpose of constructing molecular assemblies capable of undergoing photoinduced electron transfer.

Keywords: amino acids and derivatives; electron donor; electron transfer; chromophores; ruthenium complexes.

Electron transfer is one of the prototypical reactions in chemistry.[1] Interpretation of electron transfer data in solution is often made difficult by the effects of diffusion when electron transfer is rapid and diffusion is the rate limiting step. A method to overcome these limitations involves designing molecular assemblies in which an electron transfer donor (D) and electron transfer acceptor (A) are covalently bound as part of the same molecule and electron transfer is induced by the absorption of light. One approach to the design of such molecular assemblies has been based on oligoprolines that undergo photoinduced electron transfer to create long-lived Redox-separated (RS) states consisting of a chromophore, an oxidized donor and a reduced acceptor. These systems have proven to be useful for the study of intramolecular electron transfer in the absence of diffusional effects.[2]

In this paper we report the synthesis of three new amino acids, one of which is capable of functioning as an electron transfer donor and the other two amino acids as electron transfer chromophores. The electron transfer donor amino acid is designed to have a redox potential that is sufficient to quench the excited state of a chromophore, ruthenium bipyridine complex, to form a RS state as well as to have characteristic absorption features in its oxidized form necessary for detection in transient absorbance experiments.

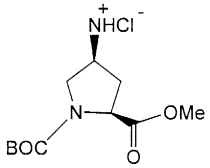
In order to modify the excited state redox potential of a well-established Ru-bpy chromphore, **6**, bipyridine ligands with electron withdrawing diethyl amides in the 4,4′-position were used (Fig. 1).

Synthesis of *n-tert*-butoxycarbonyl-*cis*-4-amino proline methyl ester (**1**) was achieved by a variation on a previously reported method which consists of five steps starting with *trans*-4-hydroxy-L-proline.[2b]

* Corresponding author. E-mail: tjmeyer@lanl.gov (T. J. Meyer III)

† Present address: Los Alamos National Laboratory, MS A127, Los Alamos, NM 87545, USA.

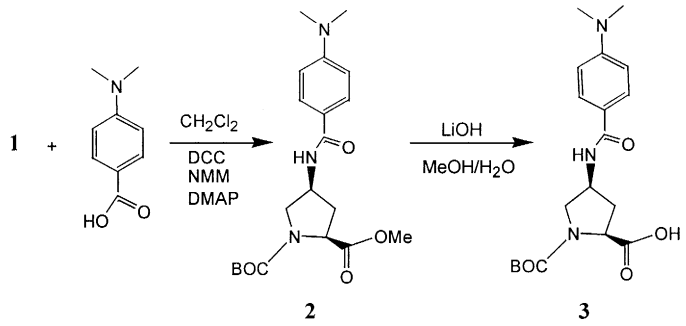
0040-4039/00/$ - see front matter
PII: S0040-4039(00)00584-0



(1)

Fig. 1.

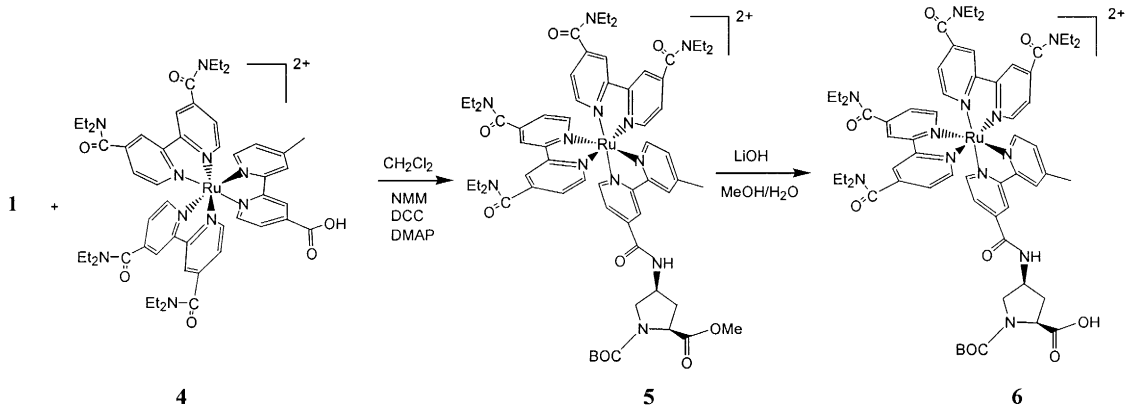
In order to separate the reduced amino proline from unreacted azide starting material, the oily product was dissolved in absolute ethanol and slowly dripped into vigorously swirling petroleum ether affording selective precipitation of only the desired product.



(1)

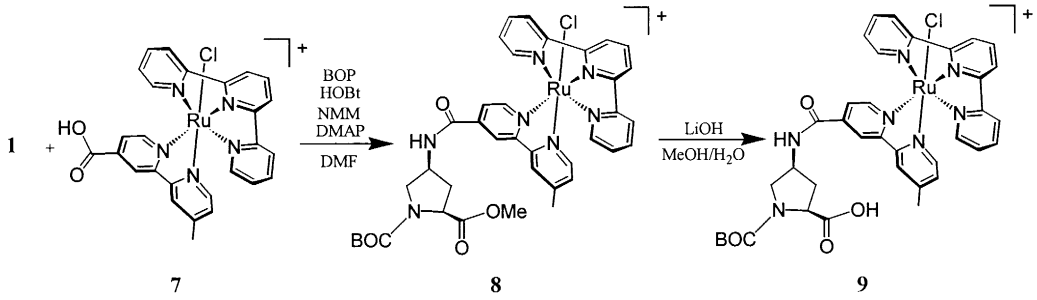
Synthesis of **3** (Eq. (1)) was achieved by first dissolving dimethylaminobenzoic acid, 4 mmol (1 equiv.), Boc protected *cis*-4-amino proline methyl ester (**1**), and *N*-methylmorpholine (NMM), 12.3 mmol (3.0 equiv.), in 75 ml dichloromethane. In the next step, solid dicyclohexylcarbamide (DCC), 4.4 mmol (1.1 equiv.) and dimethylaminopyridine (DMAP), 0.4 mmol (0.1 equiv.) were added and the mixture was stirred for 18 h. A drop of acetic acid was added and the mixture was stirred for an additional 30 min. The precipitated urea was filtered and the solvent was evaporated under reduced pressure to give a beige colored residue. This beige residue was chromatographed on a silica gel column by using a 1:1 (v/v) ethyl acetate:hexane mixture. The required fraction was collected and the solvent was evaporated to give **2** in 62% yield.[3] Compound **2** was dissolved in a 3:1 (v/v) methanol:water mixture and cooled to 0°C, then 5 equiv. of lithium hydroxide were added and the mixture stirred overnight at room temperature. Methanol was removed by rotary evaporation and 10 mL water was added. The aqueous solvent was adjusted to pH 3 with 0.1 M HCl to give a white precipitate. The solids were filtered and dried in a vacuum dessicator overnight to give **3** in 89% yield.[4]

The same coupling strategy used for **1**, 4 mmol (1 equiv.), *N*-methylmorpholine, 12.3 mmol (3.0 equiv.), solid dicyclohexylcarbodiimide, 4.4 mmol (1.1 equiv.) and dimethylaminopyridine, 0.4 mmol (0.1 equiv.) in 75 mL dichloromethane, was used to synthesize complex **5** (Eq. (2)) starting with 4 mmol of **4**.[5]



(2)

After overnight coupling, addition of a drop of acetic acid and further stirring for 30 min, the precipitated urea was removed by filtration. Removal of the solvent under reduced pressure gave the crude material which was purified on a neutral alumina column with 2:1 (v/v) acetonitrile:toluene solvent mixture as the eluent. The required fractions were collected and the solvent evaporated to give a red oil. The red oil was dissolved in a minimum quantity of acetonitrile and dripped into cold swirling ether to precipitate **5** as a bright orange powder in 51% yield.[6] The ester **5**, was saponified for 18 h with excess LiOH (5 equiv.) in a 3:1 (v/v) methanol:water mixture. The methanol solvent was evaporated and 0.1 M HPF_6 was added dropwise to the aqueous solution until precipitation was complete. The bright orange solid was collected on a medium porosity frit and washed with ether to give **6** in 85% yield.[7]



(3)

The synthesis of complex **8** (Eq. (3)) has been reported elsewhere.[8] For the coupling of **1** with **7**, dimethylformamide was used instead of dichloromethane to increase the solubility of the chloro complex **7**. Complex **9** was obtained by treating **8** with excess LiOH in a 3:1 (v/v) methanol:water mixture for 18 h at room temperature. Methanol was removed by rotary evaporation and the aqueous solvent was made just acidic with 0.1 M HCl. To this was added a saturated solution of ammonium hexafluorophosphate to precipitate dark brown **9** as the hexafluorophosphonate salt in 79% yield.[9] Complex **9** is important as a precursor to the corresponding aqua complex after solvolysis of the chloride. In related complexes, oxidation of the aqua form leads to highly reactive Ru^{IV}-oxo complexes, useful in organic transformations.[10]

The thermodynamic electron donor capability of **3** as defined by the reduction potential for its $D^{+/0}$ couple is 0.97 eV in acetonitrile versus the sodium saturated calomel electrode (SSCE) with 0.1 M [$N(n\text{-}C_4H_9)_4$]PF_6 (TBAH) as the electrolyte. The $Ru^{III/II}$ couples for ruthenium chromphores **6** and **9** are at 1.41 and 0.74 eV under the same conditions. The complexes are intense visible light absorbers with λ_{max}=464 nm (ε=18,800 M^{-1} cm^{-1}) for **6** and λ_{max}=514 nm (ε=10,600 M^{-1} cm^{-1}) for **9**. We anticipate that

these new chromophores and electron transfer donor will play important roles in the design of molecular assemblies for photochemical energy conversion in future work.

Acknowledgements

We would like to acknowledge Dr. C. M. Hartshorn for providing the precursors for complex **9**. Financial support from NSF, grant no. CHE-9705724 is also gratefully acknowledged.

References

1. (a) Marcus, R. A. *Rev. Mod. Phys.* **1993**, 65, 599. (b) Sutin, N.; Newton, M. D. *Annu. Rev. Phys. Chem.* **1984**, 35, 437. (c) Newton, M. D. *Chem. Rev.* **1991**, 91, 676. (d) Hush, N. S. *Trans. Faraday Soc.* **1961**, 57, 155. (e) Barbara, P. F.; Meyer, T. J.; Ratner, M. A. *J. Phys. Chem.* **1996**, *100*, 13 148.
2. (a) Slate, C. A.; Striplin, D. R.; Moss, J. A.; Chen, P.; Erickson, B. W.; Meyer, T. J. *J. Am. Chem. Soc.* **1998**, *120*, 4885. (b) McCafferty, D. G.; Friesen, D. A.; Danielson, E.; Wall, C. G.; Saderholm, M. J.; Erickson, B. W.; Meyer, T. J. *Proc. Natl. Acad. Sci. U.S.A.* **1996**, 93, 8200.
3. ^{1}H NMR data for **2**: 200 MHz, (CD_2Cl_2, δ) 7.65 (d, 2H) 7.20 (m, 1H), 6.68 (d, 2H), 4.78 (m, 1H), 4.34 (m, 1H), 3.75 (s, 3H), 3.60 (m, 2H), 3.01 (d, 6H), 2.50 (m, 1H), 2.02 (m, 1H), 1.39 (d, 9H). ESI-MS (calcd for $C_{20}H_{29}N_3O_5$: 392.4 Da) [M+H]+392.2 Da.
4. ^{1}H NMR data for **3**: 200 MHz, (CD_3CN, δ) 7.60 (d, 2H) 7.10 (m, 1H), 6.63 (d, 2H), 4.56 (m, 1H), 4.25 (m, 1H), 3.66 (s, 3H), 3.34 (m, 2H), 2.96 (s, 6H), 2.50 (m, 1H), 2.05 (m, 1H), 1.40 (d, 9H). ESI-MS (calcd for $C_{19}H_{27}N_3O_5$: 377.4 Da) [M+H]+377 Da.
5. Maxwell, K. A. PhD Thesis. University of North Carolina at Chapel Hill, 1999.
6. ^{1}H NMR data for **5**: 200 MHz, (CD_3CN, δ): 8.75 (s, 1H), 8.55 (s, 1H), 8.45 (s, br, 5H), 7.80 (m, 4H), 7.65 (m, 2H), 7.30 (m, 6H), 4.63 (m, 1H), 4.30 (m, 1H), 3.72 (s, 3H), 3.50 (m, 9H), 3.20 (q, 8H), 2.55 (m, 4H), 1.94 (m, 1H), 1.38 (d, 9H), 1.2 (t, 12H), 1.05 (t, 12H). ESI-MS (calcd for: $C_{63}H_{80}N_{12}O_9Ru$: 1250.37 Da) M^{2+} 1252 Da.
7. ^{1}H NMR data for **6**: 200 MHz, (CD_3CN, δ): 8.74 (s, 1H), 8.53 (s, 1H), 8.45 (s, br, 5H), 7.83 (m, 4H), 7.62 (m, 2H), 7.28 (m, 6H), 4.60 (m, 1H), 4.33 (m, 1H), 3.45 (m, 9H), 3.18 (q, 8H), 2.59 (m, 4H), 1.92 (m, 1H), 1.38 (d, 9H), 1.20 (t, 12H), 1.05 (t, 12H). ESI-MS (calcd for $C_{62}H_{78}N_{12}O_9Ru$: 1236.3 Da) M^{2+} 1236 Da.
8. Hartshorn, C. M.; Maxwell, K. A.; White, P. S.; DeSimone, J. M.; Meyer, T. J. *Inorg. Chem*. **1999**, in press.
9. ^{1}H NMR data for **9**: 200 MHz (CD_3CN, δ): 1.35/1.37 (s/s, 2H), 2.00 (m, 1H), 2.52 (m, 1H), 2.76 (s, 3H), 3.40 (m, 1H), 3.61 (m, 1H), 3.67 (s, 3H), 4.24 (m, 1H), 4.51 (m, 1H), 7.14 (d, 1H), 7.25 (t, 2H), 7.45 (d, 1H), 7.62 (d, 2H), 7.82 (d, 1H), 7.87 (t, 2H), 8.08 (t, 1H), 8.36 (d, 2H), 8.48 (d, 2H), 8.54 (s, 1H), 8.59 (s, 1H), 9.99 (d, 1H). ESI-MS (calcd for: $C_{37}H_{37}N_7O_5ClRu$: 796.316 Da) M^+ 797 Da.
10. (a) Farrer, B. T.; Thorp, H. H. *Inorg. Chem.* **1999**. (b) Ciftan, S. A.; Hondros, D. P.; Thorp, H. H. *Inorg. Chem.* **1998**, *37*, 1598. (c) Carter, P. J.; Cheng, C.-C.; Thorp, H. H. *J. Am. Chem. Soc.* **1998**, *120*, 632. (d) Catalano, V. J.; Heck, R. A.; Immoos, C. E.; Öhman, A.; Hill, M. G. *Inorg. Chem.* **1998**, *37*, 2150. (e) Stultz, L. K.; Binstead, R. A.; Reynolds, M. S.; Meyer, T. J. *J. Am. Chem. Soc.* **1995**, *117*, 2520. (f) Roecker, L.; Meyer, T. J. *J. Am. Chem. Soc.* **1986**, *108*, 4066.