Diaminoterephthalate-EDTA and -EGTA Conjugates – „Turn on“ Fluorescence Sensors for Zinc Ions

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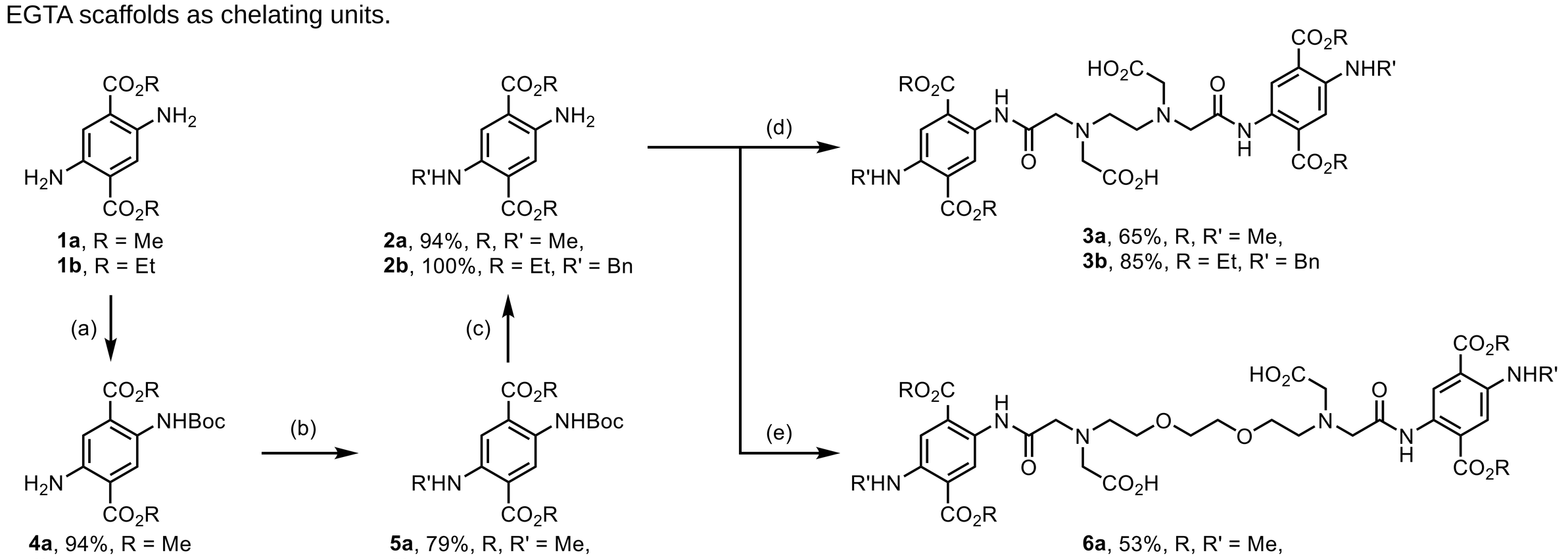
Among fluorescence dyes, diaminoterephthalates (DAT) are structural very simple compounds with remarkable fluorescence properties. Bearing two amino and carboxylate groups, the DAT motif allows a variety of functionalizations for new analytical applications.

As zinc is an essential trace element for metabolism and fulfills a variety of functions from serving as a cofactor for enzymes up to cell growth, it is of particular value to monitor zinc ions in biological matrices. Moreover, fluorescence-based analytical techniques are powerful tools for quantitative and qualitative analysis. Especially so called „turn on“ probes. Herein, we report the synthesis and spectroscopic properties of four DAT conjugates with EDTA and EGTA scaffolds as chelating units.

For the EDTA conjugates, the fluorescence intensity increases by an order of magnitude after the addition of Zn^{2+} and Sc^{3+} ions. Since Sc^{3+} is not relevant in a biological context, we found a new “turn on” sensor for the detection of Zn^{2+} ions. The coordination in solid state of the chelate complex with Zn^{2+} ions was elucidated by X-ray single crystal structure analysis of the trinuclear complex $[ZnCl_2]\{Zn(OH_2)[(DAT)_2EDTA - 2\ H]\}_2 \cdot 6.5\ H_2O$.



Scheme 1. Reagents and conditions: (a) 1.1 equiv. Boc_2O, CH_2Cl_2, 23°C, 2 d; (b) for **4a**: 1.0 equiv. MeI, 2.0 equiv. K_2CO_3, MeCN, 82°C, 16 h; for **4b**: 1.5 equiv. PhCHO, 0.5 equiv. $ZnCl_2$, 1.5 equiv. $NaBH_3CN$, CH_2Cl_2, 23°C, 16 h; (c) TFA, CH_2Cl_2, 23°C, 16 h; (d) 2 equiv. **2a** or **2b**, 1 equiv. EDTA-anhydride, DMF, 23°C, 17 h; (e) for **6a**: 1 equiv. EGTA-anhydride, 2 equiv. **2a**, DMF-MTBE (1:1), 50°C, 18 h; for **6b**: 1 equiv. EGTA-anhydride, 2 equiv. **2b**, DMF, 23°C, 20 h.

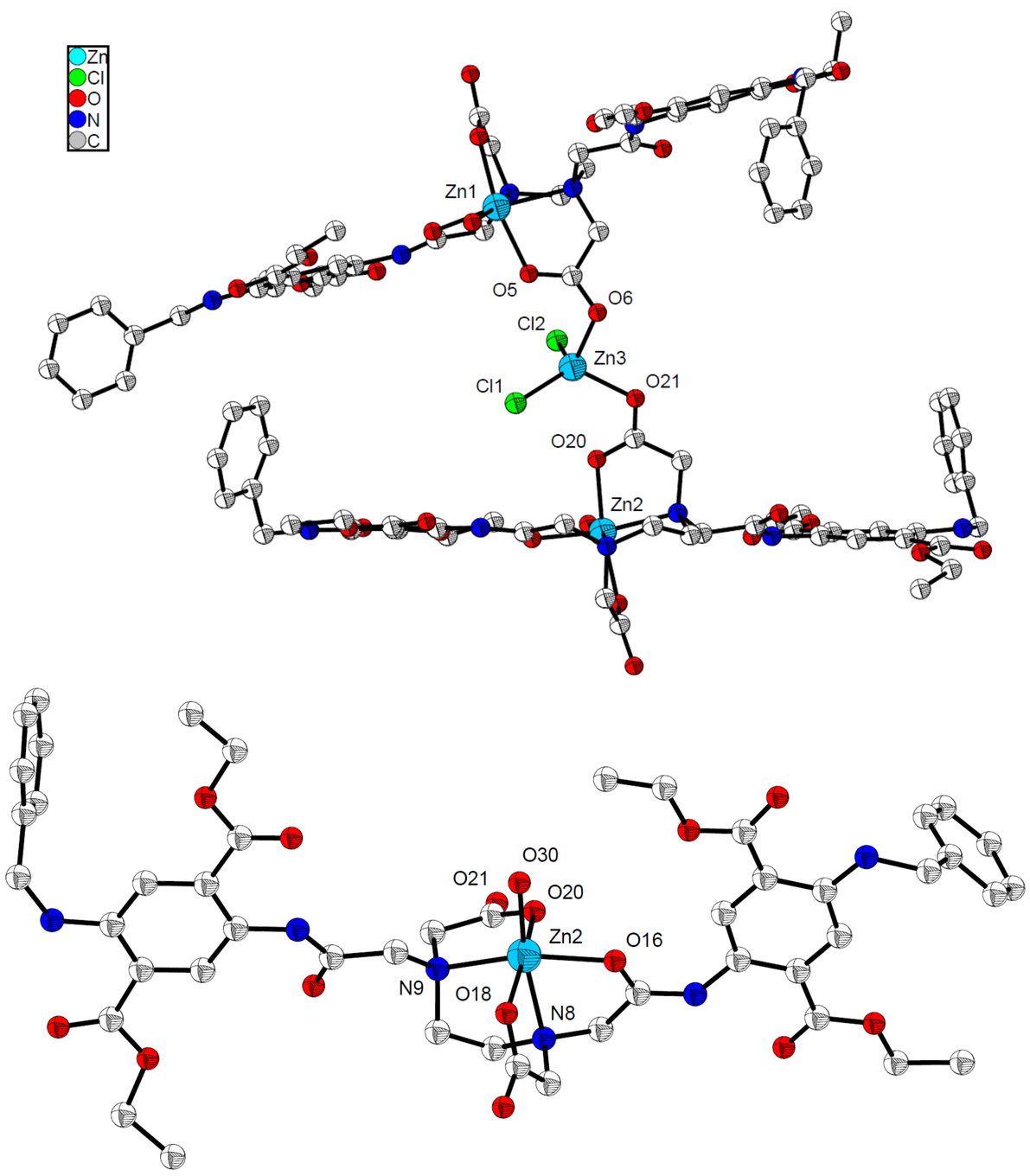


Figure 1. The ORTEP-representation of the structure of compound $[ZnCl_2][Zn(OH_2)(\mathbf{3b} - 2\ H)]_2 \cdot 6.5\ H_2O$ in the solid state.

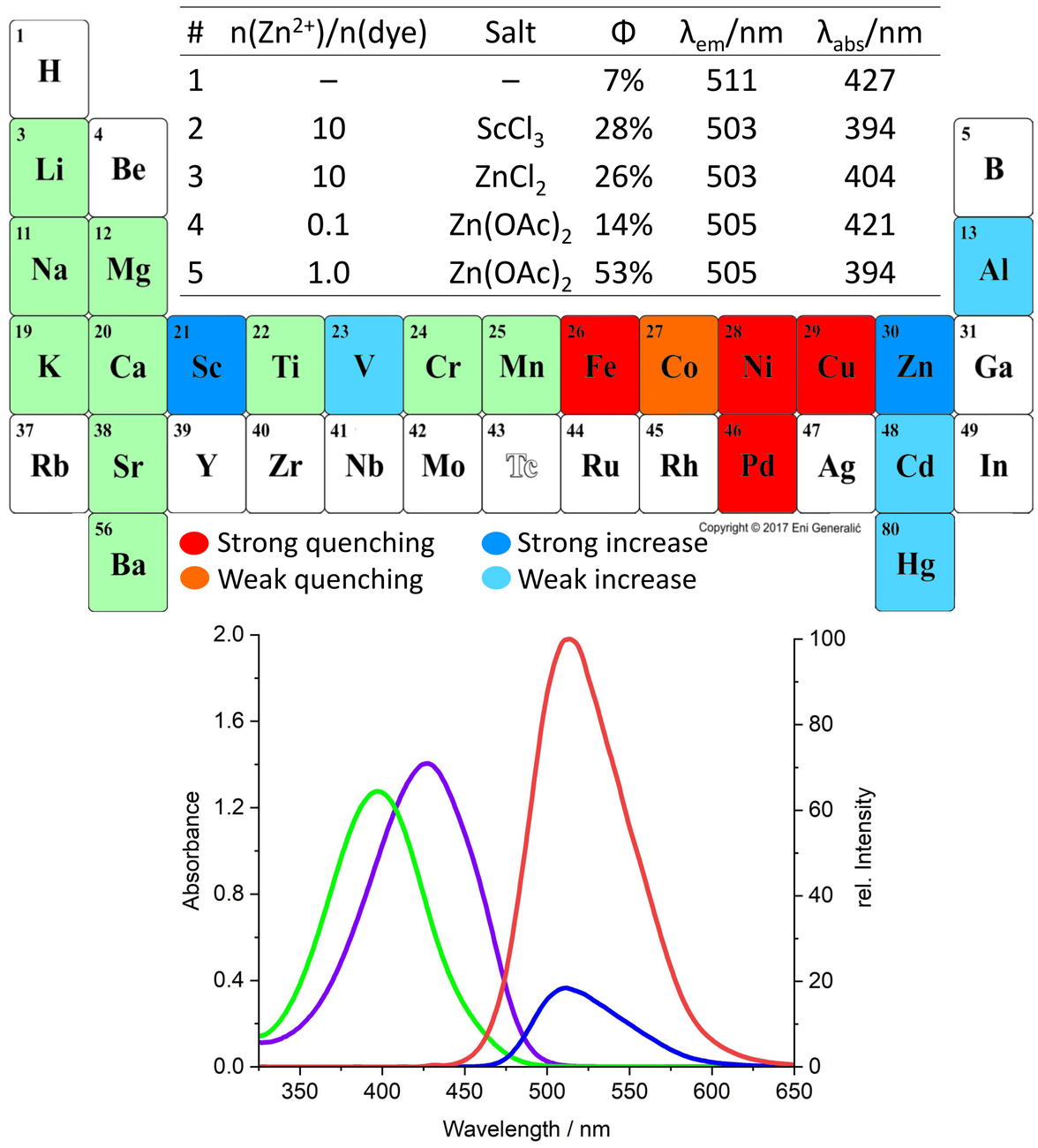


Figure 2. Changing of photophysical data by addtition of various metal chlorides to solutions of dyes **3a** and **3b** in DMSO with $n(Zn^{2+})/n(dye) = 10:1$. **3b** with $Zn(OAc)_2$ gave a small hypsochromic shift of 25 nm (purple to green line) and a six-fold increase in fluorescence intensity (blue to red line).

[1] N. Schröder, M. Schmidtmann, J. Christoffers, *Eur. J. Org. Chem.* **2021**, 4260–4268.