Water-Soluble BODIPY Dyes for Voltage Imaging

**Significance:** Previously, water solubility of BODIPY dyes was achieved through direct functionalization of the BODIPY fluorophore. Miller and co-workers report an elegant and versatile solution that does not significantly alter the dye electronics through introduction of a sulfonate on the meso-aromatic ring. These fluorophores are used to generate a series of new VoltageFluor (VF) dyes that enable the recording of action potential dynamics in neurons and cardiomyocytes.

**Comment:** The TFA-catalyzed condensation of aldehydes with pyrroles in the synthesis of BODIPY dyes is commonly performed in CH₂Cl₂ and often reported to be low-yielding. Here, the authors optimized this reaction with their sulfonated aldehyde, which was found to be insoluble in CH₂Cl₂ and toluene. Comparably good yields were obtained in DMF (e.g. 49% over three steps, see above). Therefore, the reported strategy for water-soluble BODIPY synthesis could be very useful for the wider community.

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**Synthesis of water-soluble BODIPY VF dyes:**

1. A. DMF, TFA
2. DDQ
3. DIPEA, BF₃⋅OEt₂
4. (O-tol)₃P

Heck reaction

B, Pd(OAc)₂

92% yield (R¹ = H)
25% yield (R¹ = OMe)

**BODIPY VF series:**

R¹ = H
Me
OMe

R² = Me
Et

R³ = H
Et
CO₂
CONHR
CN