The major bends of the San Andreas fault (SAF) in California are associated with significant variations in the along-fault topography. We demonstrate that the topography-induced perturbations in the intermediate (vertical) principal stress may enhance bending of a non-optimally oriented fault due to a rotation of the direction of the maximum shear stress in the brittle crust. The shear stress is predicted to rotate away from the maximum compression axis provided that the fault is non-vertical, the long-term fault slip is horizontal, and the fault geometry tends to evolve to a state that dissipates the least amount of the mechanical energy. The observed rotation of the fault plane due to variations in topography along the SAF is used to infer the magnitude of the in situ differential stress. Our results suggest that the average differential stress in the upper crust is of the order of 50 MPa, implying that the effective strength of the San Andreas fault is about a factor of two less compared to predictions based on the Byerlee’s law and the assumption of hydrostatic pore pressures, but is on the high end of constraints provided by the heat flow measurements.