Protein kinase C-δ (PKC-δ) and PKC-ε are reported to be effective in cancer prevention via S-thiolation-mediated mechanisms. This may be through stimulation of the pro-apoptotic, tumor-suppressive isozyme PKC-δ and/or inactivation of the growth stimulatory, oncogenic isozyme PKC-ε. We investigated oxidative regulatory responses of PKC-δ and PKC-ε to cystine dimethyl ester (CDME), a metabolic precursor of cystine, which, by inducing release of cellular cystine may stimulate apoptosis in different prostate cancer cells, PC3 and LNCaP. We observed that treatment of CDME in doses of 0.5mM and 5mM significantly induce apoptosis due to regulate concentration-dependent protein expressions and enzyme activities of both PKC-δ and PKC-ε only in prostate cancer cells. This regulation, which appears to come out as a result of PKC-δ stimulation and PKC-ε reduction, was confirmed by immunoblot analyses and specific PKC enzyme assays in immunoprecipitated samples. In addition to all determinations, inhibition of PKC-δ by small interfering RNA (siRNA) proved that CDME-induced cell death was dependent on PKC-δ in prostate cancer cells. These data demonstrated that CDME induces apoptosis by cysteinylation of both PKC-δ and PKC-ε in tumorigenic prostate epithelial cell lines compared to control cells. Cellular cystine may play a critical role in prostate cancer progression and prevention.