Ion-pair reversed-phase liquid chromatography (IP RP LC) is a popular method for analyzing oligonucleotides. The nature and concentration of ion-pairing agents (mobile phase modifiers) on oligo chromatographic resolution was systematically investigated and the results will be presented in our poster. Triethylamine (TEA) in aqueous hexafluoroisopropanol (HFIP) is a commonly used ion-pairing system for LC with mass spectrometry (MS) detection. This buffer provides for good overall resolving power and regular retention for homo- and heterooligonucleotides. We investigated other IP systems to achieve similar or better results. Among others, dimethylbutylamine (DMBA), tripropylamine (TPA), tributylamine (TBA), and hexylamine (HA) were investigated as acetate salts. IP efficiency increases with the hydrophobicity and concentration of the pairing agent. The IP efficiency also improves the regularity in resolution of heterooligonucleotides. The best results were obtained with TPA and HA, approaching the resolution of TEA-HFIP system; however, the MS signal is still less than with the TEA-HFIP system.