Previous research has suggested that personality traits, notably agreeableness and conscientiousness, moderate the relationship between social anxiety and alcohol-related problems. Gender differences in alcohol-related problems have also been reported in prior research. However, little is known about the contribution of gender to the explanation of associations among personality, social anxiety, and alcohol-related problems. Thus, the current study investigated how the unique and interactive associations between social anxiety, agreeableness and conscientiousness, and alcohol problems varied by gender. Participants included 512 undergraduate students who self-reported on their levels of social anxiety, personality, and alcohol-related problems. Consistent with our prior research, results of bivariate analyses revealed both agreeableness and social anxiety were significantly associated with alcohol-related problems and both explained unique variance when considered simultaneously. Contrary to hypotheses, results of multivariate regression analyses suggest that only among females personality significantly contributed to the explanation of alcohol-related problems among those with higher levels of social anxiety. Specifically, among women with higher levels of social anxiety, lower levels of agreeableness were associated with increased alcohol-related problems. Results underscore the importance of considering gender differences when examining the interactive contribution of personality to alcohol-related problem risk factors such as social anxiety. Indeed, findings of the current study suggest that among those experiencing social anxiety with lower levels of agreeableness gender is an important contributing factor with regard to risk for alcohol-related problems.