This paper is conducted to compare the determinants of profitability of the domestic and foreign Islamic banks operating in Malaysia. The Generalized Least Square (GLS) is employed with unbalanced panel data on seventeen Islamic banks, using quarterly data for the period of 2007 to 2010. In order to find out the differences in the profitability determinants, the sample of banks is divided into two sub-samples (domestic and foreign). The results reveal that domestic Islamic banks are more profitable than foreign Islamic banks. The results also show that the profitability determinants of domestic banks are different from those of foreign banks. The overhead expenses, loans, efficiency, gross domestic product growth rate and bank size have a significant effect in determining banks’ profitability, in which case applicable to the domestic banks only. In turn, the gross domestic product per capita has a significant effect in determining banks’ profitability of only the foreign banks. The study finds that, deposits, capital and reserves, inflation and banks’ age have a significant effect in determining banks’ profitability of both domestic and foreign banks. Meanwhile, liquidity and concentration are not able to explain the variability of domestic and foreign Islamic banks’ profitability. The findings indicate that the profitability of domestic banks is affected by the global financial crisis while, the profitability of foreign banks is not affected. © 2012, Econjournals. All rights reserved.