A contract between Commodore Cornelius Vanderbilt, a United States businessman, and the Nicaraguan government was signed on August 26, 1845, granting Vanderbilt's company - the Accessory Transit Company - exclusive rights to build a transisthmian canal within twelve years. The contract also gave Vanderbilt exclusive rights, while the canal was being completed, to use a land-and-water transit route across Nicaragua, part of a larger scheme to move passengers from the eastern United States to California. The westbound journey across Nicaragua began by small boat from San Juan del Norte on the Caribbean coast, traveled up the Río San Juan to San Carlos on Nicaragua Lake, crossed the lake to La Virgin on the west shore, and then continued by railroad or stagecoach to San Juan del Sur on the Pacific coast. In September 1849, the United States-Nicaragua treaty, along with Vanderbilt's contract, was approved by the Nicaraguan Congress.

British economic interests were threatened by the United States enterprise led by Vanderbilt, and violence erupted in 1850 when the British tried to block the operations of the Accessory Transit Company. As a result, United States and British government officials held diplomatic talks and on April 19, 1850, without consulting the Nicaraguan government, signed the Clayton-Bulwer Treaty, in which both countries agreed that neither would claim exclusive power over a future canal in Central America nor gain exclusive control over any part of the region. Although the Nicaraguan government originally accepted the idea of a transit route because of the economic benefit it would bring Nicaragua, the operation remained under United States and British control. Britain retained control of the Caribbean port of San Juan del Norte, and the United States owned the vessels, hotels, restaurants, and land transportation along the entire transit route.

At this time new circumstances caused problems for Nicaraguan politics and transportation across the isthmus: the filibustering activities of William Walker. On 6 May 1854 with his mercenaries he invaded Nicaragua which was torn by a civil war, pacified the country, defeated an invading army from Costa Rica, and in June 1856 was elected president of Nicaragua. Other Central American states refused to accept this "Yankee mercenary," and invaded Nicaragua from all sides. British warships blockaded Nicaraguan ports to prevent supplies from reaching Walker. The United States sent the warship St. Marys to demand that Walker surrender. On 1 May 1857 Walker capitulated, and with 463 Americans was deported to San Francisco. Three years later Walker made a final effort. In 1860 with 100 men he invaded Honduras and quickly captured the city of Trujillo. Promptly the British warship Icarus placed Trujillo under its guns and forced Walker to surrender. The British commander delivered Walker to the Honduras, and on 12 September 1860 William Walker was executed by a firing squad. Walker's actions were strongly motivated by the desire to gain control of the Accessory Transit Company and its attendant potential fortune for himself and his associates. When Walker was invading Nicaragua, he had seized the Accessory Transit Company's lake and river steamers. When in 1856 Vanderbilt regained stock control of the Transit Company, Walker claimed that the Transit Company had defrauded Nicaragua of millions of dollars, so he canceled its contract, seized its assets and closed the route. He waited until Garrison could organize a new company, The New Nicaragua Steamship Company, and could place the Sierra Nevada (1,250 tons) on the Pacific side and the Orizaba (1,450 tons) on the Caribbean side, to move merchandise. But the Canal Company tried to block the construction of the new ships. After the completion of the Panama Railway in January 1856 made use of the Nicaraguan route unprofitable.