TOTAL SYNTHESIS OF TOMAYMYCIN AND PROTHRACARCIN BY USE OF PALLADIUM CATALYZED CARBONYLATION

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Pyrrolo-1,4-benzodiazepine antibiotics, such as anthramycin, tomaymycin and neothramycin, contain a carbinol amine or imine function at position N10-C11. Our synthetic approach to these antibiotics was designed to be the formation of pyrrolo-1,4-benzodiazepine nucleus using palladium catalyzed carbonylation developed by us and the selective reduction of the corresponding amides 4 and 5 to imines 6 and 7 with $NaBH_4$ followed by treatment with silica gel as shown in Scheme. The structure of prothracarcin(7a), which was a novel antitumor antibiotic, was determined to be E-form represented as 8-dehydroxy-7-demethoxy-pretomaymycin by the respective syntheses of its E- and Z-isomers. The total synthesis of naturally occurring E-tomaymycin(7c) and its olefinic geometrical isomer, Z-tomaymycin(6c) was achieved in a similar manner.