NEW SYNTHESIS OF 1,4-BENZODIAZEPINE DERIVATIVES VIA PALLADIUM CATALYZED CARBONYLATION

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Palladium catalyzed carbonylation of aryl and vinyl halide has been developed by us as a useful method for the synthesis of heterocyclic compounds. This method was further extended to the synthesis of 1,4-benzodiazepine skeleton from o-bromoaniline derivatives 3 derived from amino acid 2. Thus, compound 4a and 4b were prepared by use of this method, which were useful intermediates for the synthesis of diazepine metabolites (dl-cyclopeptine, dl-cyclopenin and dl-cyclopenol) and diazepam. A formal synthesis of anthramycin and a total synthesis of SEN-215 have been achieved by application of this palladium catalyzed carbonylation.

On the other hand, one step synthesis of 1,4-benzodiazepinone derivatives [4a, 4d (l-cyclopeptin), 4e and 4f] from o-haloaniline (1) and amino acids (glycine, l-phenylalanine, l-proline and pipecolinic acid, respectively) was performed under several atom pressure of carbon monoxide.