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3-ARYL-2-METHYLSERINES III. SYNTHESIS VIA ALANINE AZLACTONE

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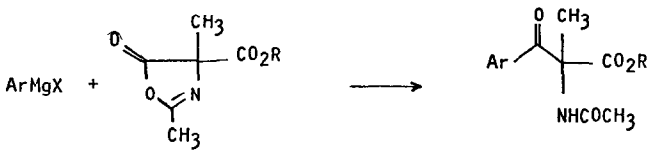
The synthesis of N-acetyl-2-aroylalaninates via addition of an aryl Grignard to the alkoxycarbonyl azlactone I was the basic step in the recently described synthesis of 3-aryl-2-methylserines[1]. Reduction of II provided both erythro and threo isomers which,

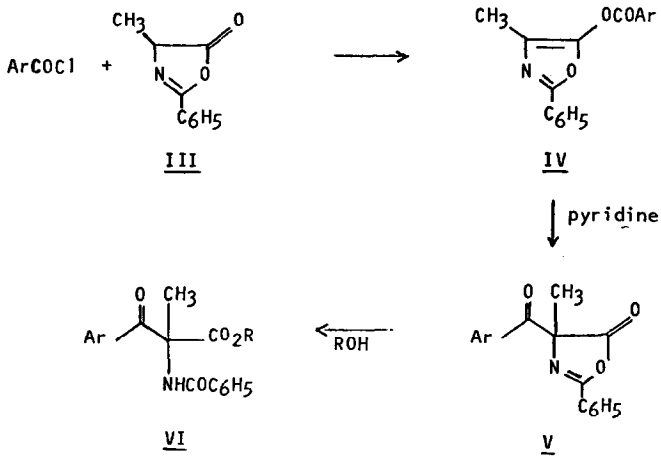


I II

when hydrolyzed, gave the respective isomeric serines.

We wish to report now an alternative general synthesis of the same class of compounds. This approach provides ready access to those members whose aromatic moiety is more readily accessible as a carboxylic acid chloride than as a Grignard reagent.

The key steps are shown schematically and described briefly[2] for both isomers of the parent 2-methyl-3-phenylserine:



III IV V VI

Benzoyl chloride was added to an equimolar solution of N-benzoylalanine azlactone (III) and triethylamine in tetrahydrofuran. Removal of the solvent and partition between chloroform and dilute acid gave 5-benzoyloxy-4-methyl-2-phenyloxazole (IV), mp 115-118°, in 63-70%. The oxazole IV, when warmed in pyridine, rearranged[3] to the azlactone V. The latter could be crystallized from cold methanol (mp 81-84°) or could be converted directly (70-78% over the two steps) to methyl N,2-dibenzoylalaninate (VI) by allowing it to stand at room temperature in methanol. VI was obtained crystalline from ether, mp 114-116°, after chromatography on silica. Chemical (sodium borohydride) or catalytic reduction (Pd/carbon) of VI gave a mixture of the two methyl N-benzoyl-2-methyl-3-phenylserinates, also separated by chromatography. The erythro (mp 104-106°) and threo (mp 144-146°) isomers provided the respective serines upon hydrolysis. The latter two steps gave yields comparable to those reported[1] for the N-acetyl analogs.

This and other examples of the synthesis will be detailed in a later publication.

References

(1) S. H. Pines, S. Karady and M. Sletzinger, J. Org. Chem., 33, 1758 (1968).

(2) New compounds showed the expected spectral properties and gave satisfactory combustion analyses.

(3) As with the aliphatic analogs: W. Steglich and G. Höfle, Angew. Chem., International Edition, 7, 61 (1968).