

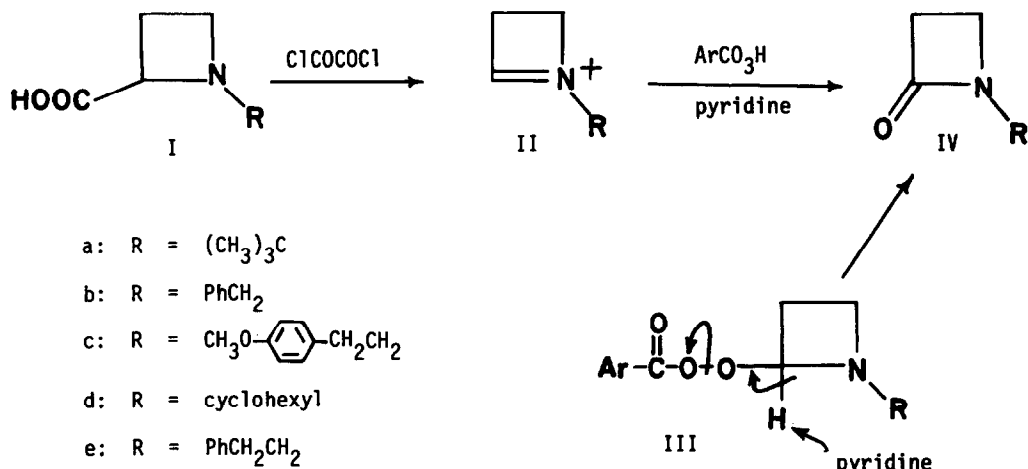
β -LACTAMS FROM AZETIDINE CARBOXYLIC ACIDS BY
PERACID REACTION WITH IMINIUM SALTS.

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We have recently reported that β -lactams may be formed from azetidine-2-carboxylic acids by low temperature dianion oxygenation.¹ We now describe a more convenient, alternative procedure for accomplishing the same conversion, making use of the reactivity of iminium salts toward nucleophiles.²⁻⁹ In particular, this method permits lactam formation in the presence of active (e.g. benzylic) hydrogens in the residue attached to nitrogen, a limitation in the earlier procedure.

Our method involves the treatment of the azetidine carboxylic acid (I) with oxalyl chloride at 0°, to form the salt (II).^{3,4} This product is then allowed to react with *m*-chloroperbenzoic acid in the presence of two equivalents of pyridine in the cold, yielding the corresponding β -lactam (IV). We suggest that the intermediate formed is the addition product (III) of the peracid anion to the iminium salt. It is quite probable that the peresters (III) undergo rapid fragmentation in the presence of pyridine to form the lactams in yields of 70-80%. Azetidinones IVa-e were characterized by comparison with authentic materials, independently prepared.



The method is exemplified by the preparation of N-benzyl-2-azetidinone. N-benzyl-2-azetidine carboxylic acid (2 mmol) prepared from γ -butyrolactone^{1,10} was added slowly to excess oxalyl chloride at 0°, followed by gradual warming to 45° (10 min). The clear solution was then poured into cold, anhydrous ether, acidified with 10 drops of 70% perchloric acid and filtered to give N-benzyl-2-azetidinium perchlorate (95%). A suspension of this iminium salt in 10 ml of methylene chloride at 0° was treated with 1 equiv. of 100% *m*-chloroperbenzoic acid¹¹ followed by 2 equiv. of pyridine.^{12,13} The resulting reaction mixture was stirred for 40 min, and then poured into water. The organic layer was separated, washed with 5% NaHCO₃, and dried over Na₂SO₄. Evaporation of the solvent under reduced pressure afforded N-benzyl-2-azetidinone (IVb) as the sole product (70%).

We are exploring the application of this oxidative decarbonylation reaction to the formation of amides from other types of α -tertiary amino acids.

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References and Notes

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2. Iminium salts are synthetically useful intermediates which provide reactive sites for attack by many types of nucleophile. Recently, a convenient method for preparing these salts from α -tertiary amino acids has been reported, along with examples of their utility in synthesis.³
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13. In the absence of pyridine the reaction was sluggish. After 48 hr, although some β -lactam was formed, at least 50% of the starting iminium salt was still present.