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REACTION BETWEEN α-LACTAMS AND GRIGNARD REAGENTS

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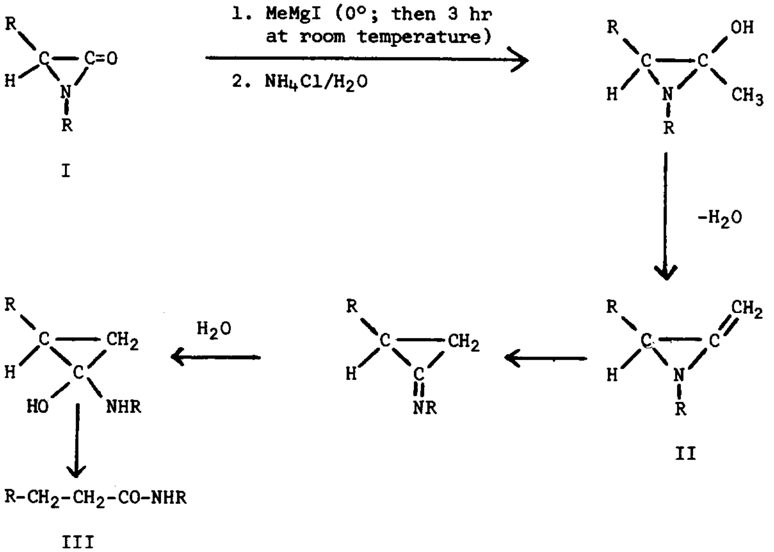
The reaction between methylmagnesium iodide and 1,3-di-<u>tert</u>-butylaziridinone (Ia) was described by Sheehan and Nafissi[2] to afford a novel, insertion-type product (IIIa) in 80% yield. No intermediates were isolated, but the following mechanism was postulated to account for the rearranged product:



a. R = *tert*-Bu

b. R = 1-adamantyl

Our interest in α-lactams[3] has led us to study the above and related reactions, and we report here a different experience with these reactions.

In our initial experiments, we allowed equimolecular amounts of phenylmagnesium bromide (prepared from triply sublimed magnesium) and the α-lactam Ib[4] to react under the conditions mentioned by Sheehan and Nafissi.[2] Although an intermediate analogous to II is impossible in this reaction, we were surprised to isolate a product devoid of aromatic hydrogens. This compound gave a positive Beilstein test, and, upon treatment with potassium tert-butoxide in ether, it furnished the familiar α-lactam Ib. By direct comparison with an authentic sample,[4] we identified the product as the bromoamide IVa (yield = 78%).

R-CHX-CO-NHR

IV

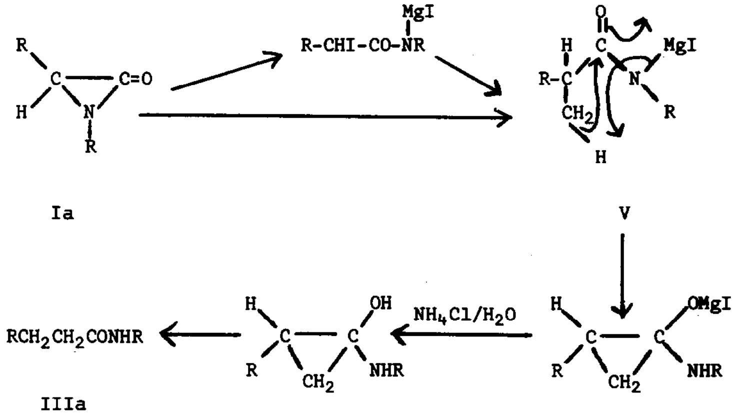
a, R = 1-adamantyl, X = Br

b, R = tert-Bu, X = I

The reaction between vinylmagnesium bromide in tetrahydrofuran and Ib under similar conditions also yielded IVa in 73% yield.

We then turned our attention to the reaction between Ia and methylmagnesium iodide. Under the conditions described by Sheehan and Nafissi (and a slow stream of argon), the main product in the crude reaction mixture does not exhibit the nmr spectrum (60 Hz, $CDCl_3$) attributed to IIIa, but instead has absorptions at 71 (9 H, singlet), 82 (9 H, singlet), 248 (1 H, singlet) and 345 Hz (1 H, broad s). After recrystallization from heptane and methanol, this compound (mp 168-170°) gives a positive Beilstein test, has ir absorption ($CHCl_3$) at 1510, 1665, and 3410 cm^{-1}, and its 70 ev mass spectrum shows m/e 297 and a prominent peak at m/e 170. Its elemental analysis agrees with the formula $C_{10}H_{20}INO$, and upon treatment with potassium tert-butoxide in ether at 0°, it is converted into Ia. We, therefore, assign structure IVb to this product. Although the nmr spectrum of the crude reaction mixture does indicate the presence of at least two products, we have not succeeded in isolating IIIa as the main product in two independent laboratories, despite taking several precautions and effecting a number of variations in the experimental procedure. In fact, when the reaction mixture is kept always at or below 0° (at about -77° during the addition of the α-lactam) and the magnesium derivative decomposed by the addition of water or a saturated solution of ammonium chloride after the reaction mixture has warmed up to 0°, IVb is almost the exculsive product, and can be isolated in 80% yield.

We wondered whether IVb (in the form of its magnesium derivative) is an intermediate in the conversion of Ia to IIIa. If so, this conversion may be envisaged as possibly proceeding through another intermediate (V) (<u>via</u> a bicyclic transition state) which may or may not be formed directly from Ia:



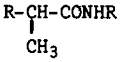
Ia

V

IIIa

R = <u>tert</u>-Bu

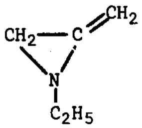
To this end, we have treated IVb as well as VI[5] [mp 147.5-148° in a sealed tube; ir (CHCl$_3$) 3429, 1660, 1500 cm^{-1}; nmr (60 Hz, CCl$_4$) 58 (9 H singlet), 81 (9 H singlet), 63 (3 H, a doublet the right half of which is obscured by the <u>tert</u>-butyl signal), 108 (1 H, quartet, J_{CH_3-H} = 7.2 Hz), 319 (1 H, broad singlet) Hz] separately with methylmagnesium



$$R-\underset{\substack{| \\ CH_3}}{CH}-CONHR$$

VI, R = <u>tert</u>-Bu

iodide, but we have failed to isolate any IIIa from these reactions. If the cyclic compound IIa were to be involved as a discrete intermediate in the conversion of Ia to Sheehan's product (IIIa), its formation would be the only example of a reaction of α-lactams in which the ring is not cleaved. Since the analogous, albeit simpler, compound VII is not only isolable but



VII

capable of surviving alkaline conditions well above room temperature,[6] an independent synthesis of IIa and a study of its reaction with aqueous ammonium chloride at room temperature should furnish strong evidence in favor of or against the mechanism proposed by Sheehan and Nafissi.

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REFERENCES

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   (c) holder of an Undergraduate Research Participation fellowship from the National Science Foundation at Wichita State University, Summer, 1970.

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