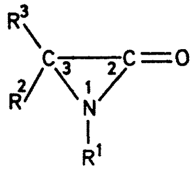
Reactions of Aziridinones with Magnesium Compounds

By ERACH R. TALATY,*† AUBRY E. DUPUY, JUN., and CLIFFORD M. UTERMOEHLEN

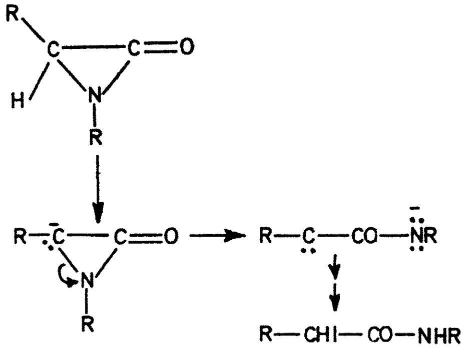
(*Departments of Chemistry of* †*Wichita State University, Wichita, Kansas* 67208; *and Louisiana State University in New Orleans, Lakefront, New Orleans, Louisiana* 70122)

Summary The reaction of 1,3-bis-(1-adamantyl)aziridin-2-one with magnesium chloride, bromide, or iodide affords the corresponding α-halogeno-amide by cleavage of the alkyl–nitrogen bond, whereas reaction of the same aziridinone with magnesium methoxide yields an α-amino-ester by cleavage of the acyl–nitrogen bond.

THE most stable aziridinones known are of type (Ia),[1] of which almost all known reactions have been effected at or above room temperature, though Sheehan and Nafissi[2] report that treatment of (Ib) with methylmagnesium iodide in ether, first at 0° and then at room temperature, affords $Me_3C{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}NHCMe_3$ (II) as the result of a novel insertion-type alkylation. We have failed to isolate (II) from this reaction. Even when all reagents were carefully purified, triply sublimed magnesium was used, and the reaction was carried out under argon or purified nitrogen in a dry apparatus equipped with an acetone–Dry Ice condenser to minimize loss of ether, there was no clear evidence of the presence of (II) in an n.m.r. spectrum of the crude reaction mixture. Instead, the product isolated in yields up to 80% is (IIIa).[3] This reaction may involve direct ring-opening of (Ib) by magnesium iodide, a possible component of the initial reaction mixture (the Schlenk equilibrium), or perhaps an abstraction of the proton at C-3 by some alkylmagnesium species, followed by or concurrent with heterolytic rupture of the 1–3 bond to produce



(Ia) $R^1 = R^2 =$ t-alkyl, $R^3 = H$
(Ib) $R^1 = R^2 = Bu^t$, $R = H$
(Ic) $R^1 = R^2 =$ 1-adamantyl, $R^3 = H$



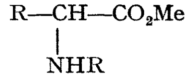
R·CHX·CO·NHR
(III)a; $R = Bu^t$, $X = I$
b; $R =$ 1-adamantyl, $X = Br$
c; $R =$ 1-adamantyl, $X = I$
d; $R =$ 1-adamantyl, $X = Cl$

a carbene, which is trapped by a species containing iodine. Subsequent hydrolysis of the reaction mixture leads to (IIIa). (In the structures shown, discrete carbanions are written for the sake of simplicity.) We report evidence in favour of the former pathway, and results of the reaction of aziridinone (Ic)[1b] with several magnesium compounds under mild conditions.

The addition of a solution of (Ic) in dry ether (1·54 mmoles in 10 ml) at 0° to magnesium bromide etherate[4] (1·93 mmoles) in ether (10 ml), prepared from triply sublimed magnesium, under nitrogen over a period of 15 min, followed by stirring at 0° for 15 min, yielded, after hydrolysis with a saturated solution of ammonium chloride, a solid, m.p. 222—224° (83% yield), identical with an authentic sample[‡] of (IIIb).[1b] Similar treatment of (Ic) with magnesium iodide etherate gave the amide (IIIc) (87%) [m.p. 248—250° (decomp.) (from CCl_4); i.r. ($CHCl_3$) ν_{max} *ca.* 3466 and 1660 cm^{-1}; 60 MHz ^{1}H n.m.r. ($CDCl_3$) τ 7·68—8·68 (m, 30H), 6·03 (s, 1H), and 4·20—4·59 (br s, 1H); M^+ 453]. This compound gave a positive result in the Beilstein test, and upon treatment with potassium t-butoxide in ether at 0°, it was completely converted into the aziridinone (Ic). When anhydrous magnesium chloride[5] (1·93 mmoles) in freshly purified tetrahydrofuran (10 ml) was allowed to react with (Ic) (1·54 mmoles) in tetrahydrofuran (5 ml) at 0° for 190 min under dry nitrogen, there was obtained the amide (IIId) (78%) [m.p. 204—206° (from n-heptane); i.r. (CCl_4) ν_{max} *ca.* 3405 and 1673 cm^{-1}; 60 MHz ^{1}H n.m.r. ($CDCl_3$) τ 7·58—8·62 (m, 30H), 6·09 (s, 1H), and 4·30—4·75 (br s, 1H); M^+ 361, 363]. This compound also gave a positive result in the Beilstein test, but it was converted only partially into (Ic) by treatment with potassium t-butoxide, even in boiling ether. Thus, the magnesium halides bring about a ready cleavage of the alkyl–nitrogen bond in the aziridinones (Ib) and (Ic). These reactions can be useful in organic syntheses. For example, one of the common methods for the preparation of α-iodo-carboxylic acids or their derivatives (the displacement of a chlorine or bromine atom in the corresponding α-chloro- or α-bromo-compounds by the iodide ion) is not applicable to the preparation of (IIIa) or (IIIc) because it would involve displacement at a neopentyl carbon atom. Hence, the following sequence illustrates a convenient method for effecting such halogen-exchange reactions.

$$\text{(IIIb)} \xrightarrow[Et_2O]{KOBu^t} \text{(Ic)} \xrightarrow[Et_2O]{MgI_2} \text{(IIIc)}$$

The mode of cleavage of the aziridinone ring can vary considerably with the type of magnesium compound. Thus, the reaction of (Ic) (1·54 mmoles) with freshly prepared magnesium methoxide (1·93 mmoles) in dry ether (15 ml) under reflux for 2·5 h under dry nitrogen afforded, after filtration and extraction of the residue with methylene chloride, the ester (IV) (75%) [m.p. 135—136° (from n-heptane); i.r. (CCl_4) ν_{max} *ca.* 3320 and 1730 cm^{-1}; 60 MHz ^{1}H n.m.r. (CCl_4) τ 7·67—9·02 (m, 31H including N–H), 7·14 (s, 1H), and 6·28 (s, 3H); M^+ 357] by cleavage of the acyl–nitrogen bond.



$$R\text{—}\underset{\displaystyle NHR}{\underset{|}{CH}}\text{—}CO_2Me$$

(IV) R = 1-adamantyl

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[‡] The m.p. reported (202—204°) in ref. 1b is a misprint.

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