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Reactions of 2,4-Azetidinedione with Nucleophilic Reagents

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Synopsis. The reaction of 2,4-azetidinedione with a variety of nucleophiles was compared with that of *N*-methylsuccinimide. 2,4-Azetidinedione gave ring-cleaved addition products, while *N*-methylsuccinimide afforded simply addition products to the carbonyl group.

It is known that imide compounds show a variety of reactivity with nucleophilic reagents depending on their structures.[1] For instance, *N*-phenylsuccinimide reacts with ethylmagnesium bromide to give 2-ethyl-2-hydroxy-1-phenylpyrrolidine (**1**), while arylmagnesium bromides react with *N*-substituted maleimides to yield *N*-substituted 5-aryl-5-hydroxy-2-pyrrolidones (**2**) (See Fig. 1).[2] Under certain conditions, the imide ring is cleaved by the Grignard reagent, *i.e.*, *N*-methyl keto amide was the product of the reaction of *N*-methylsuccinimide with ethylmagnesium bromide.[3] Diphenyl and diethyl substituted *N*-phenylmalonimides react with three equivalents of aryl Grignard reagents to give the disubstituted *N*-phenylacetamides and the tertiary alcohols derived from the Grignard reagents.[4]

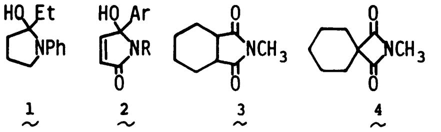
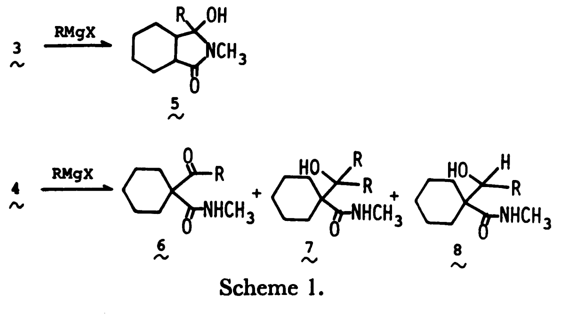


Fig. 1.

Recently, the authors[5] reported photochemistry of *N*-methyl-*cis*-1,2-cyclohexanedicarboximide (**3**), which afforded four-membered ring imide, 2,4-azetidinedione **4**.[6] In this report, the reaction of this photoproduct **4** with some nucleophiles has been studied and compared with the reactivity of succinimide **3**.

Results and Discussion

Reactions of **3** and **4** with various Grignard reagents (RMgX) were summarized in Scheme 1 and Table 1. Grignard reagents reacted with **3** to give the hydroxy lactams **5**. The yields of **5** were fairly good. The corresponding reaction of **4** afforded ring-cleaved products **6**, **7**, and **8**. The *β*-keto amide **6** was the primary product and an excess amount of Grignard reagents reacted with keto carbonyl group of **6** to give the double alkylated products **7** and the reduced products **8**. Because the primary product **6** is sterically hindered by the tertiary carbon, reduction of **6** to **8** occurs mainly when R is bulky. Especially when *R*=*i*-Pr, *t*-Bu, octyl, and cyclohexyl, reduction products **8** (**8c**, **8e**, **8f**, and **8g**) were exclusively produced and none of double alkylation products **7** was detected.



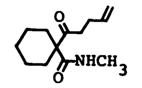
Scheme 1.

Table 1. Yield of the products in the reaction of **3** and **4** with Grignard reagents

	R in RMgX	Reaction of **3** Yield of **5**/%	Reaction of **4** Yield of **6**/%	Yield of **7**/%	Yield of **8**/%
a	Me	85	11	63	—
b	Et	99	4	44	52
c	*i*-Pr	96	—	—	85
d	*n*-Bu	95	6	12	79
e	*t*-Bu	47	—	—	50
f	Octyl	95	—	—	96
g	Cyclohexyl	96	—	—	92
h	Ph	97	—	99	—
i	Allyl	95	—	72	—
j	Vinyl	84	—	9 (**7k**,[a] 90)	—

a)

7k:



The difference of the reactions between **3** and **4** may be explained as follows. Grignard reagents attack one of the carbonyl carbons of the imide **3** to form the five-membered ring intermediate. The same type of the intermediate is perhaps produced in the reaction of **4**. Since ring strain of four-membered ring is larger than that of five-membered ring, the four-membered ring intermediate could immediately isomerize to the ring-cleaved intermediate,[4] the precursor of **6**, **7**, and **8**.

Reductions of **3** and **4** with sodium borohydride of lithium aluminum hydride proceeded similarly. The imide **3** was reduced to the hydroxy lactam **5**, (R=H), while the imide **4** gave the formyl amide **6**, (R=H). Here, it seems to be general that four-membered imides are ring-cleaved but five-membered imides are not cleaved in the course of the reaction.

When lithium reagents were used as the nucleophile, a new reaction was observed. Thus, phenyllithium reacted with **3** to give the ring-cleaved keto amide **9** as well as **5h**. The imide **4** afforded the amide **10** with addition of an excess amount of phenyllithium in the reacting mixture (See Fig. 2). The lithium reagent is a stronger base than the Grignard reagent and also **3** has a hydrogen at the position adjacent to the carbonyl group. These facts may cause the difference between the reactions of Grignard reagents and lithium reagents. The formation of **10** may be explained by retro-Aldol type reaction. Actually, treatment of **7h** with phenyllithium afforded the same product **10** and triphenylmethanol.

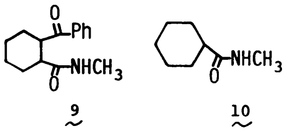


Fig. 2.

It is general that only one of the carbonyl carbons of imides photochemically behaves like a simple ketone.[7] In the present study, it is realized that ring size of cyclic imides strongly affects its chemical reaction pathway.

References

1) M. K. Hargreaves, J. G. Pritchard, and H. R. Dave, *Chem. Rev.*, **70**, 439, (1970).

2) A. Queen and A. Reipas, *J. Chem. Soc.*, **1967**, 245.

3) R. Lukev and Z. Linhartova, *Collect. Czech. Chem. Commun.*, **25**, 502, (1960).

4) W. Flitsch and R. Heidhues, *Z. Naturforsch.*, *β*, **21**, 1137, (1966).

5) K. Maruyama, T. Ishitoku, and Y. Kubo, *J. Org. Chem.*, **46**, 27, (1981).

6) N. H. Cromwell and B. Phillips, *Chem. Rev.*, **79**, 331, (1979).

7) a) K. Maruyama and Y. Kubo, *J. Org. Chem.*, **42**, 3215, (1977). b) K. Maruyama and Y. Kubo, *J. Org. Chem.*, **46**, 3612, (1981) and references sited therein. c) Y. Kanaoka, *Acc. Chem. Res.*, **11**, 407, (1978).