The Reaction of 1-Methoxycarbonyl-2-imidazolidone with Phenylmagnesium Bromide

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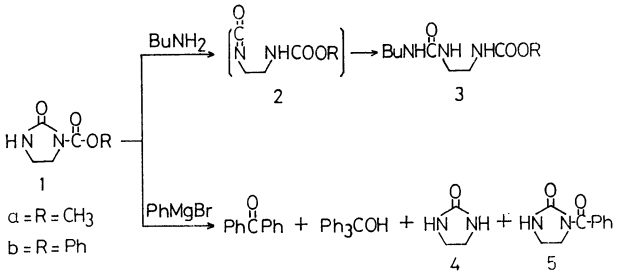
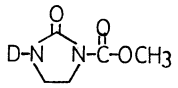
Synopsis. It is found that 1-methoxycarbonyl- or 1-phenoxycarbonyl-2-imidazolidone reacts with phenylmagnesium bromide to afford benzophenone and triphenylmethanol, together with 2-imidazolidone, by nucleophilic attack on the carbonyl group at the side chain.

The reaction of 1-methoxycarbonyl- or 1-phenoxycarbonyl-2-imidazolidone (**1a** or **1b**) with nucleophiles is of interest in relation to the reactivity of a carboxylated biotin coenzyme transferring the carboxylato group to Ac–CoA in a biological system.[1] Recently we have reported that the reaction of Compound **1a** with butylamine proceeds via the formation of an isocyanate intermediate (**2**) by ring opening to afford *N*-butylcarbamoyl-*N'*-methoxycarbonylethylenediamine (**3a**) in a quantitative yield.[2] In the course of our studies of the reactivity of Compound **1**, we have found that phenylmagnesium bromide undergoes nucleophilic attack on the carbonyl group of **1a** and **1b** to afford benzophenone, triphenylmethanol, and 1-benzoyl-2-imidazolidone (**5**). Herein, we wish to report our findings on these reactions.



Scheme 1.

The reactions of Compounds **1a** and **1b** with phenylmagnesium bromide in tetrahydrofuran were carried out by stirring under argon at room temperature for 2 h. At the **1a**/phenylmagnesium bromide molar ratio of 1:1, benzophenone, triphenylmethanol, 2-imidazolidone and **5** were obtained in low yields, with an almost entire recovery of **1a**, as Table 1 shows. The low yields of the products is caused by the consumption of phenylmagnesium bromide for abstracting the hydrogen of the NH group of **1**. This was established by the fact that, in the reaction of 1-methoxycarbonyl-2-imidazolidone-3-*d* (**6**) with 1-naphthylmagnesium bromide in the molar ratio of 1:1, naphthalene-1-*d* is produced in a 90% yield. When the **1a**/phenylmagnesium bromide molar ratio of 1:3 was used, benzophenone and triphenylmethanol were obtained in higher yields, without the formation of any methyl benzoate, as Table 1 shows. No products by ring opening were obtained at all. The formation of benzophenone was observed also in the reaction with **1b**. However, it was difficult to isolate Compound **4**



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in amounts corresponding to those of benzophenone and triphenylmethanol, since it was very soluble in water. In addition to these products, Compound **5** was obtained, though in a low yield. Thus, it became apparent that the reactions of Compounds **1a** and **1b** with phenylmagnesium bromide result in the fission of the N–COOMe bond.

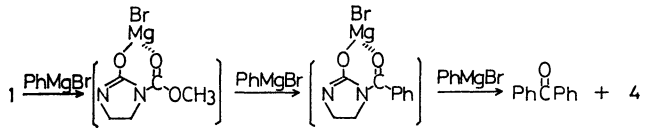
The difference in reactivity between butylamine and phenylmagnesium bromide led us to consider that the chelation of the Mg^{2+} ion after the abstraction of the hydrogen of the NH group of **1** prevents ring opening and brings about the nucleophilic attack of phenylmagnesium bromide on the side chain (Scheme 2). Furthermore, benzophenone is regarded as being formed *via* the intermediary formation of Compound **5** rather than methyl benzoate on the basis of the following results: 1) Methyl benzoate is not detected in the reaction of **1** with phenylmagnesium bromide; 2) the reaction of Compound **5** with phenylmagnesium bromide under similar conditions affords benzophenone and triphenylmethanol in good yields, together with the formation of Compound **4**, as Table 1 shows; 3) the reaction of a mixture (1:1) of **1a** and methyl benzoate with phenylmagnesium bromide (3 equiv.) affords benzophenone, triphenylmethanol, **4**, and **5** in 42, 1, 17, and 7% yields respectively, with a 94% recovery of methyl benzoate.

As has been described above, it became apparent that phenylmagnesium bromide can cleave the N–COOR bond by the assistance of the Mg^{2+} ion, unlike the behavior of butylamine, and that this behavior of the Mg^{2+} ion is similar to that in the butylamine/Mg^{2+}-ion system, bringing about the cleavage of the N–COOR bond.[3]

TABLE 1. THE YIELDS OF THE PRODUCTS IN THE REACTIONS OF **1** AND **5** WITH PHENYLMAGNESIUM BROMIDE[a]

Compd	Compd/PhMgBr Molar ratio	Yield/% PhCOPh	Ph_3COH	**4**	**5**
1a[b]	1 : 1	6	1	11	5
1a	1 : 3	42	15	22	4
1b[c]	1 : 3	63	5	35	6
5	1 : 2	75	8	40	

a) Concentration of Compounds **1** and **5**: 6.81 mmol in 25 cm^3 of tetrahydrofuran. b) Recovery %=81%. c) Phenol was obtained in a 56% yield.



Scheme 2.

Experimental

Materials. *1-Methoxycarbonyl-2-imidazolidone (**1a**)*: Compound **1a** (mp 178—179 °C) was prepared by the method described in our previous paper.[2]

*1-Benzoyl-2-imidazolidone (**5**)*: A solution of 16.3 g (0.116 mol) of benzoyl chloride in 20 cm³ of dry benzene was added, under nitrogen, to a solution of 10 g (0.116 mol) of **4** in 50 cm³ of dry benzene at room temperature; the solution was stirred under reflux for 20 h and then cooled to room temperature. The crystals thus deposited were collected by filtration, washed with water, and recrystallized from chloroform to give 19.9 g (90%) of **5**: mp 167—168 °C; IR (KBr) 3220 (NH), 1733, 1670 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ=3.62(t, 2H, $-CH_2-$), 4.25(t, 2H, $-CH_2-$), 5.78 (bs, 1H, NH), and 7.29—7.8 (m, 5H, aromatic); Found: C, 63.12; H, 5.18; N, 14.69%, Calcd for $C_{10}H_{10}N_2O_2$: C, 63.15; H, 5.30; N, 14.73%.

*1-Methoxycarbonyl-2-imidazolidone-3-*d *(**6**)*: A mixture of 2 g (13.9 mmol) of **1a** and 20 cm³ of D_2O was refluxed for 2 h and then evaporated to dryness under reduced pressure. The white residue was dried again under reduced pressure at 100 °C to yield **6**. The **6** exhibited an IR (KBr) peak at 2480 cm^{-1} (N–D) and 1760, 1670 cm^{-1} (C=O) and the complete disappearance of the NMR ($CDCl_3$) signal of N–H at δ 6.45, although the other signals were the same as those of **1a**.

*Reaction of 1-Methoxycarbonyl-2-imidazolidone-3-*d *with 1-Naphthylmagnesium Bromide.* A solution of 1.576 g (6.81 mmol) of 1-naphthylmagnesium bromide in 10 cm³ of tetrahydrofuran was added, drop by drop and at room temperature, to a solution of 0.988 g (6.81 mmol) of 1-methoxycarbonyl-2-imidazolidone-3-*d* in 15 cm³ of tetrahydrofuran, and then the mixture was stirred for 2 h. The resulting mixture was treated by a method similar to that used in the case of **1a** to yield 0.791 g (90%) of naphthalene-1-*d* (**7**). The IR (KBr) signals of **7** coincided with those of the authentic specimens. MS *m/e*, 129 (M^+). Another product, **1a**, was isolated from the acidic solution in an 87% yield.

Reaction with Phenylmagnesium Bromide. *Compound **1a***: A solution of 3.7 g (20.43 mmol) of phenylmagnesium bromide in 10 cm³ of tetrahydrofuran was added under argon to a solution of 0.982 g (6.81 mmol) of **1a** in 15 cm³ of tetrahydrofuran, after which the mixture was stirred at room temperature for 2 h. The resulting mixture was acidified with a dilute hydrochloric acid with ice, and the solution was extracted with ether and then chloroform. The ether and chloroform solutions were combined and dried over magnesium sulfate. After the removal of the ether and chloroform *in vacuo*, the residue was chromatographed on a silica-gel column, using chloroform as the eluent, to give 0.521 g (42%) of benzophenone, 0.266 g (15%) of triphenylmethanol, and 0.052 g (4%) of **5**. The aqueous layer was evaporated *in vacuo*, and the residue was chromatographed on a silica-gel column, using methanol and ethanol as the eluents, to give 0.127 g (13%) of **1a** and 0.129 g (22%) of **4**. The products were identified by a comparison of their melting points and IR, ^{1}H NMR, and mass spectra with those of the respective authentic specimens.

*Compounds **1b** and **5***: The reaction of **1b** and **5** with phenylmagnesium bromide and the isolation of the reaction products were carried out by a method similar to that used in the case of **1a**.

References

1) a) J. Moss and M. D. Lane, *Adv. Enzymol.*, **35**, 321 (1971), and the references cited therein; b) M. C. Scrutton and M. R. Young, "The Enzymes," ed by P. D. Boyer, Academic Press, New York (1972), Vol. 6, pp. 1—35, and the references cited therein.

2) N. Matsumura, Y. Yagyu, H. Kawai, Y. Otsuji, and E. Imoto, *Nippon Kagaku Kaishi*, **1977**, 362.

3) N. Matsumura, H. Kawai, Y. Otsuji, and E. Imoto, *Bull. Chem. Soc. Jpn.*, **50**, 2417 (1977).