A FACILE SYNTHESIS OF 2,4-OXAZOLIDINEDIONES

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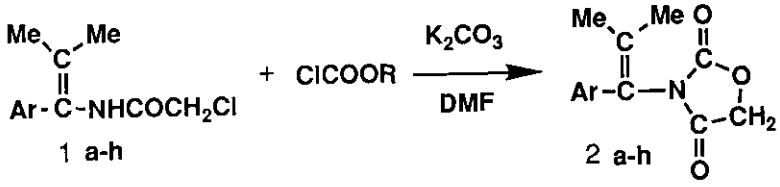
Abstract —— 2,4-Oxazolidinediones bearing 1-aryl-2-methylpropen-1-yl substituent at 3-position were obtained easily by the reaction of 2-chloro-*N*-(1-aryl-2-methyl-1-propenyl)acetamides with both chloroformic acid ester and potassium carbonate in DMF.

2,4-Oxazolidinediones are useful as biologically active compounds such as antiepileptic drugs[1] and fungicides.[2] It is well known that one of the general synthesis of 2,4-oxazolidinediones is accomplished by the action of isocyanates on α-hydroxy acid in the presence of sodium.[3] In the course of the studies of a reaction on 2-chloro-*N*-(1-phenyl-2-methyl-1-propenyl)acetamide (**1a**), we found that **1a** was converted into 2,4-oxazolidinedione having 2-methyl-1-phenylpropen-1-yl substituent at 3-position in the presence of chloroformic acid ester and potassium carbonate in DMF. In this paper, we wish to report a new, facile synthesis of 2,4-oxazolidinediones having 1-aryl-2-methyl-1-propenyl moiety at 3-position. 3-(1-Aryl-2-methylpropen-1-yl)-2,4-oxazolidinediones (**2**) were obtained by the reaction of 2-chloro-*N*-(1-aryl-2-methylpropen-1-yl)acetamides (**1**) with chloroformic acid ester, such as methyl chloroformate, as shown in Scheme 1. The starting amides (**1**) were prepared from *N*-(1-aryl-2-methyl)propanimines and chloroacetyl chloride.

Scheme 1



A typical procedure is as follows. To a 100 ml flask was added 2-chloro-*N*-[1-(4-methoxyphenyl)-2-methylpropen-1-yl]acetamide (**1c**) (2.55 g, 10 mmol), methyl chloroformate (1.18 g, 13 mmol), potassium carbonate (1.45 g, 11 mmol) and DMF (30 ml). The mixture was heated in an oil bath (80 °C) for about 3 h. After cooling to room temperature, the reaction mixture was washed with water and aqueous potassium carbonate. The organic portion was extracted with ether. The ether layer was dried over sodium sulfate. After removal of the solvent, the resulting viscous liquid was purified by column chromatography

on silica gel to afford a pale yellow solid (1.64 g, 63%) of 3-[1-(4-methoxyphenyl)-2-methyl-1-propenyl]-2,4-oxazolidinedione (Table 1, **2c**). ^{1}H-Nmr (δ ppm in $CDCl_3$): 1.74(3H, s, CH_3), 1.82(3H, s, CH_3), 3.75(3H, s, OCH_3), 4.64(2H, s, CH_2), 6.82(2H, d, J=9 Hz, aromatic H), 7.27(2H, d, J=9 Hz, aromatic H); ir (KBr) 1810 and 1745 cm^{-1} (C=O); ms m/z 261(M^+); Anal. Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.36; H, 5.84; N, 5.10.

Table 1. 2,4-Oxazolidinediones (**2**)

No.	Ar	Yield/%	mp(°C)	ir(cm^{-1})
a	C_6H_5	74	108	1810, 1730
b	4-MeC_6H_4	48	122	1810, 1730
c	4-$MeOC_6H_4$	63	85	1810, 1745
d	4-ClC_6H_4	45	123	1810, 1740
e	4-FC_6H_4	48	85	1810, 1750
f	2-C_4H_3O	43	101	1820, 1740
g	2-C_4H_3S	69	87	1830, 1755
h	5-Me-2-C_4H_2S	71	88	1820, 1745

These results are summarized in Table 1. As can be seen in the Table, 2,4-oxazolidinediones were obtained in nice yields by use of methyl chloroformate as a chloroformic acid ester. When other chloroformic acid esters such as isopropyl chloroformate and phenyl chloroformate were employed for this type of reaction, the yield of **2a** was 31% and 32%. On the other hand, the reaction of **1a** with potassium carbonate and methyl chloroformate was carried out by using acetone as a solvent instead of DMF, **2a** was not obtained and **1a** was recovered. When the reaction of **1a** with ethyl chlorothioformate was carried out, **2a** was similarly produced in the yield of 52%. In the absence of chloroformic acid ester, a small amount of **2a** was given by the reaction of **1a** with potassium carbonate in DMF. However, the reaction with other bases such as triethylamine in place of potassium carbonate, did not afford **2a** at all. The effects of potassium carbonate and DMF on the reaction are not clear at the present time.

The reaction described in this paper was found to be applicable to the reaction of a variety of 2-chloroacetamides. The detailed study on the mechanism as well as the application of this reaction is now in progress.

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