HETEROCYCLES, Vol. 27, No 9, 1988

REACTION OF ISOCYANIC ACID AND ISOCYANATES WITH DIKETENE. PREPARATION OF 2H-1,3-OXAZINES, 4-PYRONES, AND 2-PYRIDONES[1]

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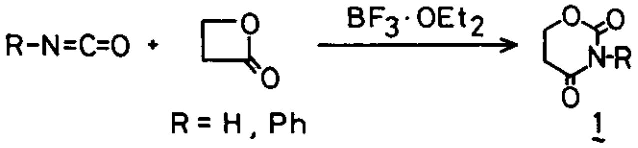
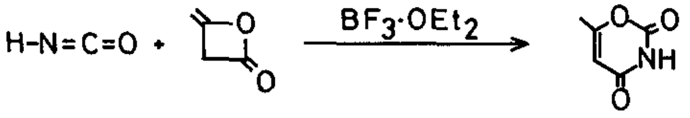
Abstract— Reaction of diketene with isocyanic acid gave the expected product, 2,4-dioxo-6-methyl-3,4-dihydro-2H-1,3-oxazine (2), but with aryl isocyanates gave 3-aryl-2,4-dioxo-6-methyl-3,4-dihydro-2H-1,3-oxazines (3), 3-(arylcarbamoyl)-2,6-dimethyl-4-pyrones (4), and 3-acetyl-1-aryl-4-hydroxy-6-methyl-2-pyridones (5) depending on the reaction conditions.

During studies on isocyanic acid and its derivatives, we have reported that reaction of β-propiolactone with isocyanic acid and phenyl isocyanate in the presence of boron trifluoride etherate ($BF_3 \cdot OEt_2$) gave 2,4-dioxo-3,4,5,6-tetrahydro-2H-1,3-oxazine (1) (Scheme 1).[2] The reaction was regarded as the formal insertion reaction of a isocyanato group into the oxygen-carbonyl bond of the lactone ring. With the aim of extending the scope of the reaction to obtain the corresponding 2,4-dioxo-6-methyl-3,4-dihydro-2H-1,3-oxazine derivatives, we treated isocyanic acid and aryl isocyanates with diketene in the place of β-propiolactone. In this communication, we mainly describe the unexpected results in the reaction of aryl isocyanates with diketene.



Scheme 1

According to the previous procedure,[2] isocyanic acid was treated with 1 eq of diketene in the presence of $BF_3 \cdot OEt_2$ (0.01 eq) to give the expected 2,4-dioxo-6-methyl-3,4-dihydro-2H-1,3-oxazine (2) as colorless crystals [mp 225°C (dec.)] in 7% yield (Scheme 2). In case of reaction of aryl isocyanates with diketene, p-toluenesulfonic acid (p-TsOH) was mainly used as acid catalysts. A solution of isocyanates and diketene (1.5 eq) in



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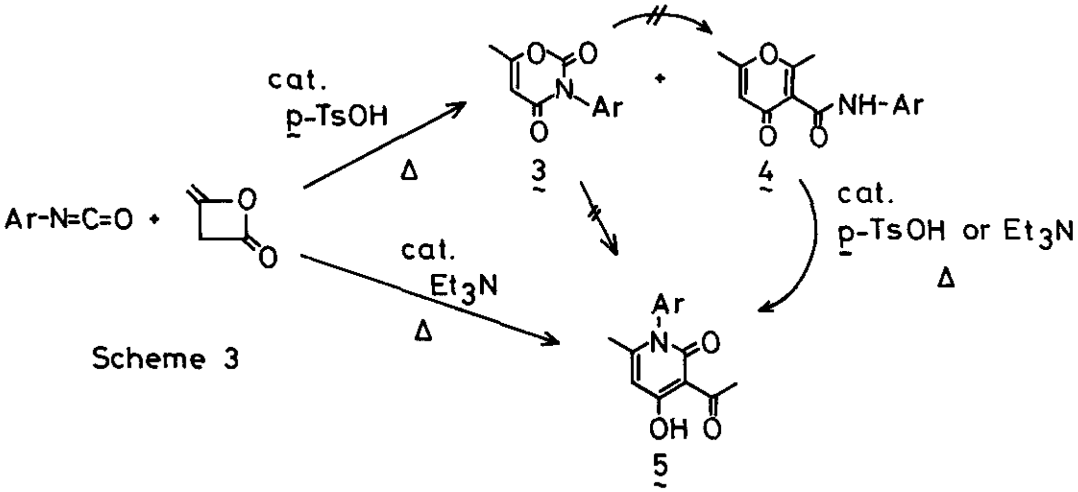
Scheme 2

toluene was heated at 110-115°C in the presence of p-TsOH (0.01 eq). Not only the desired product, 2,4-dioxo-6-methyl-3-aryl-3,4-dihydro-2H-1,3-oxazine (3) but also 3-(arylcarbamoyl)-2,6-dimethyl-4-pyrones (4) was obtained (Table 1 and Scheme 3). Substituents on the aromatic ring caused to change the ratio of products 3 and 4. Ortho substituents seem to hinder the formation of 3,4-dihydro-2H-1,3-oxazine 3. By contrast, isocyanates were allowed to react with diketene (2.0 eq) in the presence of triethylamine (0.015 eq) to afford 3-acetyl-1-aryl-6-methyl-4-hydroxy-2-pyridones (5) in yields described in Table 2. By use of basic catalyst, 1,3-oxazines 3 or 4-pyrones 4 could not be isolated. Independent experiments showed that 3 were not converted to 4 or 5 under the reaction conditions. However, acid- or base-induced thermal isomerization easily converted the isolated 4 into 5 (Scheme 3).



Scheme 3

In literatures there were reported that reaction of primary arylamines with diketene in the presence of tert. amine as catalysts gave N-substituted 3-acetyl-4-hydroxy-6-methyl-2-pyridones 5[3,4] and that treatment of arylamines with acetoacetate derivatives in the presence of polyphosphoric acid afforded 4-pyrones 4 as a by-product of 4-hydroxyquinaldines.[5] In both cases, acetoacetamides were regarded as important reaction intermediates and were isolated. Since the present reaction was carried out under anhydrous conditions, however, it was not considered that acetoacetamides existed in the reaction mixture (Indeed, we could not detect acetoacetamides in the reaction medium.).[6]

Table 1. Preparation of 2H-1,3-Oxazines 3 and 4-Pyrones 4.

	R	Catalyst	Oxazine 3	Yield (%)[a]	Pyrone 4	Yield (%)[a]
a	Ph	p-TsOH	3a	41	4a	20
b	2-ClPh	p-TsOH	3b	-	4b	35
c	3-ClPh	p-TsOH	3c	38	4c	trace
d	4-ClPh	p-TsOH	3d	69	4d	-
e	2,5-Cl_2Ph	p-TsOH	3e	82	4e	-
		$BF_3\cdot OEt_2$		16		14
f	2-NO_2Ph	p-TsOH	3f	26	4f	7
g	3-NO_2Ph	p-TsOH	3g	12	4g	51
h	4-NO_2Ph	p-TsOH	3h	94	4h	-
i	2-MePh	$BF_3\cdot OEt_2$	3i	-	4i	60
j	4-MePh	p-TsOH	3j	55	4j	7
		$BF_3\cdot OEt_2$		-		10

All the new compounds have the satisfactory ^{1}H nmr, ir and analytical data supported the described structures.

a: Isolated yield.

Table 2. Preparation of 2-Pyridones 5.

	R	Pyridone 5	Yield (%)[a]
a	Ph	5a	65
b	2-ClPh	5b	35
c	3-ClPh	5c	34
d	4-ClPh	5d	81
e	2,5-Cl_2Ph	5e	66
f	2-NO_2Ph	5f	53
g	3-NO_2Ph	5g	37
h	4-NO_2Ph	5h	60
i	2-MePh	5i	-
j	4-MePh	5j	52

All the new compounds have the satisfactory ^{1}H nmr, ir and analytical data supported the described structures.

a: Isolated yield.

According to the present procedure, we can easily obtain different heterocycles from the same starting materials in moderate to good yields depending on the reaction conditions. Thus the reaction may provide a new promising route to various types of 1,3-oxazines 3, arylcarbamoyl-4-pyrones 4 and N-aryl-2-pyridones 5. Details on mechanistic studies of the reaction will be reported in the near future.

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6. Reaction of phenyl isocyanate with diketene in the presence of water gave diphenylurea and a small amount of N-phenyl-2-pyridone **5a** accompanied by 3-phenylcarbamoyl-4-pyrone **4a**. Under the reaction conditions described in the text, no amount of diphenyl urea was detected.

Received, 18th April, 1988