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Formation and Reaction of Acyl Substituted Nitrile Ylide through the $Rh_2(OAc)_4$-Catalyzed Reaction of α-Diazocarbonyl Compounds with Benzonitrile

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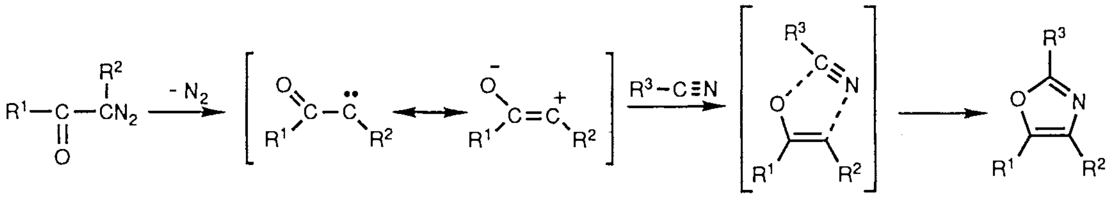
The rhodium(II) acetate-catalyzed reaction of α-diazocarbonyl compounds with benzonitrile and dimethyl acetylenedicarboxylate gave oxazoles and pyrrole-3,4-dicarboxylates through the 1,5-cyclization and 1,3-dipolar cycloaddition of the acyl substituted nitrile ylide intermediates generated by the reaction of ketocarbenoids with benzonitrile.

Chemistry of nitrile ylide has long received attention of organic chemists from the synthetic and theoretical points, and many methods have been developed for the generation of nitrile ylide.[1)] One of the most important method is the reaction of carbenoid with nitrile. However, only a few papers have been reported for the formation of the acyl substituted nitrile ylide. For example, Huisgen and his co-workers have reported that the copper-catalyzed reaction of α-diazoacetophenone in the presence of benzonitrile gave 2,5-diphenyloxazole together with products through the Wolff rearrangement.[2)] They explained the formation of the oxazole by the concerted 1,3-dipolar cycloaddition of intermediate ketocarbenoid toward nitrile group.[3)] However, generation of nitrile ylide was proposed recently in the reaction of carbene with nitrile on the basis of the spectroscopic studies.[4)]



The author has studied the formation of acyl substituted carbonyl ylides[5)] and thiocarbonyl ylides[6)] by the reactions of carbenoid with carbonyl compounds or thiocarbonyl compounds under the catalysis of α-diazocarbonyl compounds. As an extension of our recent research, we wish to report the formation of acyl substituted nitrile ylide by the $Rh_2(OAc)_4$-catalyzed decomposition of α-diazocarbonyl compounds in the presence of nitriles, and its competitive reactions between intramolecular 1,5-cyclization and intermolecular trapping by 1,3-dipolar cycloadditions with dipolarophiles.

The rhodium(II) acetate-catalyzed decomposition of p-chloro-α-diazoacetophenone (**1d**) in benzonitrile in the presence of dimethyl acetylenedicarboxylate (DMAD) gave 5-(p-chlorophenyl)-2-phenyloxazole (**4d**) and dimethyl 2-(p-chlorobenzoyl)-5-phenylpyrrole-3,4-dicarboxylate (**5d**) in 63 and 11% yields, respectively.[7] The structure determination of the pyrrole derivative **5d** was based on the results of elemental analysis and spectroscopic properties.[8] These two products are explained by the intermediacy of nitrile ylide **A**, which gives oxazole **4** through the 1,5-cyclization and pyrrole **5** through intermolecular 1,3-dipolar cycloaddition with DMAD followed by the proton migration. The possibility of the formation of pyrrole **5** through the Diels-Alder reaction of **4** with DMAD is ruled out by the control experiment of the treatment of **4d** with DMAD in the presence of $Rh_2(OAc)_4$ at 60 °C, which did not give **5d** recovering **4d** quantitatively.

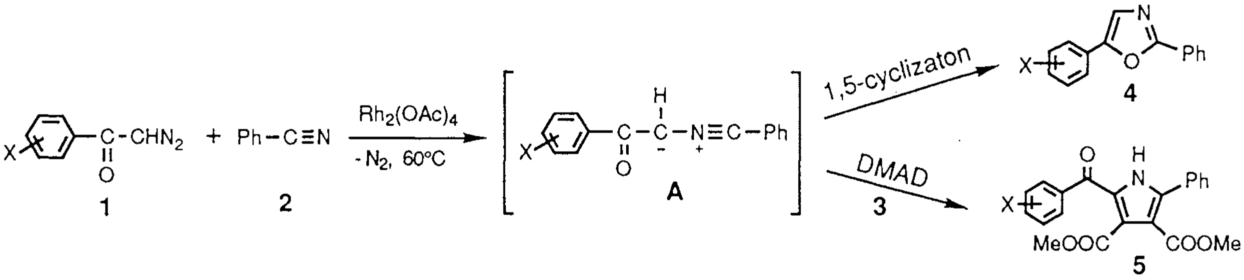
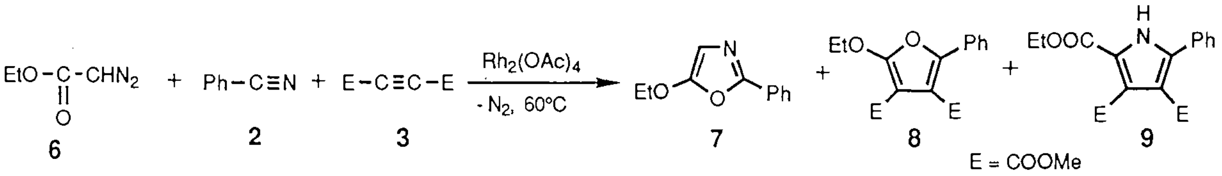


Table 1. Yields and Ratio of Products **4** and **5** in $Rh_2(OAc)_4$-Catalyzed Reaction of α-Diazoacetophenones with DMAD in the Presence of Benzonitrile

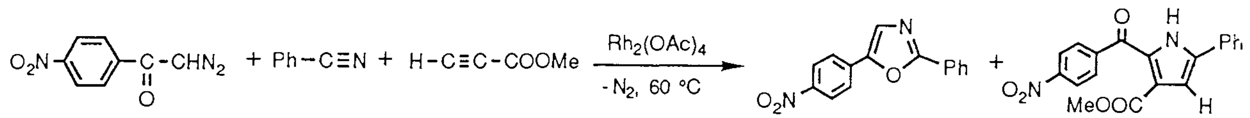
Run	Diazoacetophenone **1**	X	Yield/% **4**	Yield/% **5**	Total yield/% (**4** + **5**)	Product ratio **5**/(**4** + **5**)
a	**1a**	p-OCH_3	38.2	5.8	44.0	0.13
b	**1b**	p-CH_3	44.6	9.8	54.0	0.18
c	**1c**	H	50.6	11.0	61.6	0.18
d	**1d**	p-Cl	63.0	11.0	74.0	0.15
e	**1e**	m-Cl	62.6	15.1	77.7	0.19
f	**1f**	p-CN	60.9	9.0	69.9	0.13
g	**1g**	p-NO_2	61.2	18.3	79.5	0.23
h	**1h**	m-NO_2	60.5	12.5	73.0	0.17

The reactions of other m- and p-substituted α-diazoacetophenones gave the corresponding oxazole and pyrrole derivatives in moderate or good yields as shown in Table 1. The low yields of the products of α-diazoacetophenones with electron-donating groups such as p-methoxyl and p-methyl groups are attributed to the 1,3-dipolar cycloaddition of diazoketone **1** with DMAD[9] which reduces the generation of the nitrile ylide. The ratio of the yield of the 1,3-dipolar cycloadduct to the total yield of the products through the nitrile ylide **A**, **5**/(**4** + **5**), is affected a little by the substituents on diazoacetophenones. The catalytic decomposition of **1g** in the presence of ethylenic dipolarophiles such as maleic anhydride, N-phenyl maleimide, dimethyl fumarate, and dimethyl maleate gave the oxazole **4g** without or with a trace amount of the corresponding cycloadducts.

The reaction of ethyl diazoacetate (**6**) with benzonitrile and DMAD gave 5-ethoxy-2-phenyloxazole (**7**) and dimethyl 2-ethoxycarbonyl-5-phenyl-pyrrole-3,4-dicarboxylate (**9**) in 4.8 and 17.8% yields together with dimethyl 2-ethoxy-5-phenylfuran-3,4-dicarboxylate (**8**: 2.6% yield). Formation of **8** is explained by the Diels-Alder reaction of the oxazole **7** with DMAD followed by the retro-Diels-Alder reaction to eliminate hydrogen cyanide.[10] The ethoxyl group on C-5 of oxazole **7** accelerates the Diels-Alder reaction of the oxazole.[11] The preferred formation of intermolecular 1,3-dipolar cycloaddition product (**9**) to the intramolecular 1,5-cyclization products (**7** and **8**) is attributable to the slow 1,5-cyclization of the nitrile ylide intermediate because of the low nucleophilicity of ester carbonyl oxygen.



There are two possibilities in the 1,3-dipolar cycloaddition of the nitrile ylide **A**, when asymmetric compound is used as a dipolarophile. The reaction of p-nitro-α-diazoacetophenone (**1g**) in the presence of benzonitrile and methyl propiolate (**10**) led to an oxazole derivative **11** and a pyrrole derivative **12** in 70 and 3.8% yields, respectively. The regiochemistry of the pyrrole **12** was determined by the measurement of the differential NOE spectrum irradiating a proton on C-4 of pyrrole ring at 7.05 ppm which caused an increase of the ortho-proton signal of phenyl group on C-5.



1g 2 10 11 12

Further studies to get more informations on the regioselectivity of pyrrole formation in the reaction of other diazoacetophenones and diazoacetates are now in progress.

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7) General procedure: a PhCN (20 ml) solution of **1** (1.0 mmol) was added dropwise to a magnetic stirring solution of DMAD (20 mmol) and $Rh_2(OAc)_4$ (0.05 mmol) in PhCN (10 ml) at 60 °C under N_2 atmosphere. The reaction products were separated by medium pressure column chromatography (silica gel/hexane-ethyl acetate) after usual treatment.

8) All new compounds described in this paper gave satisfactory results of elemental analysis and spectroscopic measurement.

9) For example, dimethyl 5-(p-methoxybenzoyl)pyrazole-3,4-dicarboxylate was obtained in 25% yield in the reaction of p-methoxy-α-diazoacetophenone (**1a**). No pyrazole derivative was isolated in the reactions of other diazoacetophenones.

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