Pergamon

Tetrahedron Letters 39 (1998) 3165–3166

TETRAHEDRON
LETTERS

Stereocontrol of Metal-Catalyzed Cycloaddition of Carbonyl Ylide with *N*-Substituted Maleimide

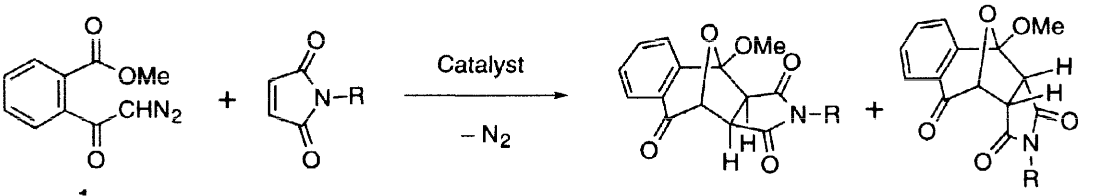
Hiroyuki Suga,*,[1] Hajime Ishida, and Toshikazu Ibata*

Department of Chemistry, Graduate School of Science, Osaka University, Toyonaka, Osaka 560, Japan

Received 14 January 1998; revised 18 February 1998; accepted 20 February 1998

Abstract: The CuOTf (20 mol%) or CuCl-Yb(OTf)$_3$ (5 mol%) catalyzed decomposition of *o*-(methoxycarbonyl)-α-diazoacetophenone in the presence of *N*-methylmaleimide gave 1,3-dipolar cycloadducts in an *endo*-selective manner (*endo* : *exo* = 94 : 6). On the other hand, the Rh$_2$(OAc)$_4$-catalyzed (5 mol%) reaction gave cycloadducts with *exo*-selectivity (*endo* : *exo* = 11 : 89).

Since we demonstrated a series of studies on the metal-catalyzed decomposition of *o*-(alkoxycarbonyl)-α-diazoacetophnone in the presence of various dipolarophiles,[2] the intramolecular carbenoid-carbonyl reaction has become one of the most effective methods for generating carbonyl ylides.[3] Our present question concerns the role of the metallic catalyst on the cycloaddition of the carbonyl ylide after its formation. Recently, Padwa[4] and Doyle[5] separately reported Rh(II) catalyst-dependent changes in chemo-, regio-, and diastereochemistry during a carbenoid-carbonyl reaction followed by carbonyl ylide formation. However, there have been no reports concerning successful stereocontrol of the metal-catalyzed cycloaddition of a carbonyl ylide. In the present communication, we report the first examples of dramatic changes in stereoselectivity caused by the metal-catalyst in 1,3-dipolar cycloaddition of carbonyl ylides with *N*-substituted maleimides.[6]



1 exo-2 endo-2

At first, we examined the decomposition of *o*-(methoxycarbonyl)-α-diazoacetophnone (**1**) in the presence of *N*-methylmaleimide by using several kinds of typical metal-catalysts (5 mol%) for the decomposition of diazo compounds (Table 1, entries 2, 3, 6, and 7). Surprisingly, when the metal-catalysts having Lewis acidity such as CuOTf (*endo* : *exo* = 87 : 13) and Cu(OTf)$_2$ (*endo* : *exo* = 82 : 18) were used, highly *endo*-selective 1,3-dipolar cycloaddition occurred as is not usually observed in the carbonyl ylide cycloadditions (entries 2 and 6). Using 20 mol% of CuOTf increased *endo*-selectivity to *endo* : *exo* = 94 : 6 (entry 1) in comparison with the result of entry 2. It is interesting that the selectivity changed to *exo* excess in the CuOTf-catalyzed reaction when 2,2'-isopropylidenebis[(4*S*)-4-*t*-butyl-2-oxazoline] was used as ligand (entry 5). On the other hand, we found that high *endo*-selectivity (*endo* : *exo* = 94 : 6) was observed by adding 5 mol% of Yb(OTf)$_3$ under 5 mol% of CuCl-catalyzed conditions (entry 4). The reaction by use of Rh$_2$(OAc)$_4$ showed the highest *exo*-selectivity (*endo* : *exo* = 11: 89) among the catalysts listed in Table 1 (entry 7). The CuOTf or CuCl-Yb(OTf)$_3$ catalyzed reaction of diazoacetophenone **1** with *N*-ethylmaleimide also showed high *endo*-selectivity (entries 8 and 9). The reaction using Rh$_2$(OAc)$_4$ showed moderate *exo*-selectivity (entry 10). Although the reactions with *N*-phenylmaleimide showed lower selectivity than that attained with *N*-methyl- and *N*-ethylmaleimides, the tendency of the selectivity is almost the same. Despite the fact that **1** was completly consumed under the conditions listed in Table 1, the moderate to low yields observed in the reaction using a Lewis acid may be due to the difficult formation of carbonyl ylides. In the case of the reactions with *N*-phenylmaleimide, dirhodium (II) tetrakis[methyl 2-pyrrolididone-5(*S*)-carboxylate] (Rh$_2$(5*S*-MEPY)$_4$) was the best catalyst to synthesize the

0040-4039/98/$19.00 © 1998 Elsevier Science Ltd. All rights reserved.
PII: S0040-4039(98)00449-3

exo-adduct selectively (entry 16). It is also interesting to point out that asymmetric induction of the reaction was observed by using 20 mol% of $Rh_2(5S\text{-MEPY})_4$ (*endo*: 20% ee, *exo*: 5% ee). Although coordination of the ligand to CuOTf showed low *exo*-selectivity (entries 14 and 15), a small degree of enantioselectivity was observed (20 mol% catalyst, *endo*: 15% ee; 5 mol% catalyst, *endo*: 6% ee). To the best of our knowledge, these are the first examples of the enantioselectivity obtained in the intermolecular carbonyl ylide cycloaddition.[7]

Table 1. Cycloadditions of Carbonyl Ylide with *N*-Substituted Maleimide in the Presence of a Catalyst [a]

Entry	R	Catalyst	Temperature	Yield,%	endo : exo [c]
1	Me	CuOTf [b]	reflux	34	94:6
2	Me	CuOTf	reflux	49	87:13
3	Me	CuCl	reflux	81	26:74
4	Me	CuCl, $Yb(OTf)_3$	reflux	52	94:6
5	Me	Ln-CuOTf [d]	reflux	81	29:71 [e]
6	Me	$Cu(OTf)_2$	reflux	24	82:18
7	Me	$Rh_2(OAc)_4$	reflux	70	11:89
8	Et	CuOTf	rt	44	82:18
9	Et	CuCl, $Yb(OTf)_3$	reflux	40	88:12
10	Et	$Rh_2(OAc)_4$	reflux	77	23:77
11	Ph	CuOTf	rt	60	63:37
12	Ph	CuCl, $Yb(OTf)_3$	reflux	43	77:23
13	Ph	CuCl, $Yb(OTf)_3$ [f]	reflux	21	90:10
14	Ph	Ln-CuOTf [d]	rt	83	43:57 [g]
15	Ph	Ln-CuOTf [b,d]	rt	53	37:63 [h]
16	Ph	$Rh_2(5S\text{-MEPY})_4$ [b]	rt	45	11:89 [i]

a) To a solution of *N*-substituted maleimide in benzene in the presence of 5 mol% of catalyst was added a solution of diazo compound **1** in benzene at the temperature cited in Table 1 over a period of 1 h and then the mixture was stirred for 30 min. b) The reaction was carried out in the presence of 20 mol% of the catalyst. c) The ratio was determined by ^1H NMR. d) Ln: 2,2'-Isopropylidenebis[(4*S*)-4-*t*-butyl-2-oxazoline] e) Almost no enantioselectivity was obtained. f) The reaction was carried out in MeCN. g) *endo*: 6% ee, *exo*: 0% ee [j] h) *endo*: 15% ee, *exo*: 0% ee [j] i) *endo*: 20% ee, *exo*: 5% ee [j] j) Determined by HPLC (Daicel Chiralpak AS).

The reason for the high *endo*-selectivity using CuOTf or CuCl-$Yb(OTf)_3$ catalysts is not clear at this point. However, the Lewis acid presumably controls the stereoselectivity in the 1,3-dipolar cycloaddition of carbonyl ylides by coordination to dipolarophiles similarly as reported in the reaction of nitrones.[6a,c]

References and Note

1. Current address: Department of Chemistry and Material Engineering, Faculty of Engineering, Shinshu University, Wakasato, Nagano 380, Japan
2. a) Ueda, K.; Ibata, T.; Takebayashi, M. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 2779. b) Ibata, T.; Jitsuhiro, K. *Bull. Chem. Soc. Jpn*, **1979**, *52*, 3582. c) Ibata, T.; Jitsuhiro, K.; Tsubokura, Y. *Bull. Chem. Soc. Jpn.*, **1981**, *54*, 240. d) Ibata, T.; Toyoda, J. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 1787.
3. Padwa, A.; Weingarten, M. D. *Chem. Rev.* **1996**, *96*, 223.
4. Padwa, A.; Austin, D. J.; Hornbuckle, S. F. *J. Org. Chem.* **1996**, *61*, 63.
5. Doyle, M. P.; Forbes, D. C.; Protopopva, M. N.; Stanley, S. A.; Vasbinder, M. M.; Xavier, K. R. *J. Org. Chem.* **1997**, *62*, 7210.
6. There are a few examples known that Lewis acids controlled regio- and/or stereoselectivity of dipolar cycloadditions. a) Kanemasa, S.; Uemura, T.; Wada, E.; *Tetrahedron Lett.* **1992**, *33*, 7889. b) Kanemasa, S. Nishiuchi, M.; Kamimura, A.; Hori, K. *J. Am. Chem. Soc.*, **1994**, *116*, 2324. c) Gothelf, K. V.; Thomsen, I.; Jørgensen, K. A. *J. Am. Chem. Soc.*, **1996**, *118*, 59. also see the references cited there in.
7. Recently, intramolecular enantioselective cycloaddition of carbonyl ylide has been reported: Hodgson, D. M.; Stupple, P. A.; Johnstone, C. *Tetrahedoron Lett.*, **1997**, *38*, 6471.