

The Carbonyl-Diels-Alder Reaction Catalyzed by Bismuth (III) Chloride

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Abstract: *In presence of bismuth (III) chloride, a carbonylated electrophile (ethyl mesoxalate or glyoxylate) and usual diene led selectively (65 to 100%) the hetero carbonyl-Diels-Alder reaction with the ene reaction product. BiCl₃ exhibits strong catalytic activity and, compared with previous literature, reacts under mild conditions.* © 1998 Elsevier Science Ltd. All rights reserved.

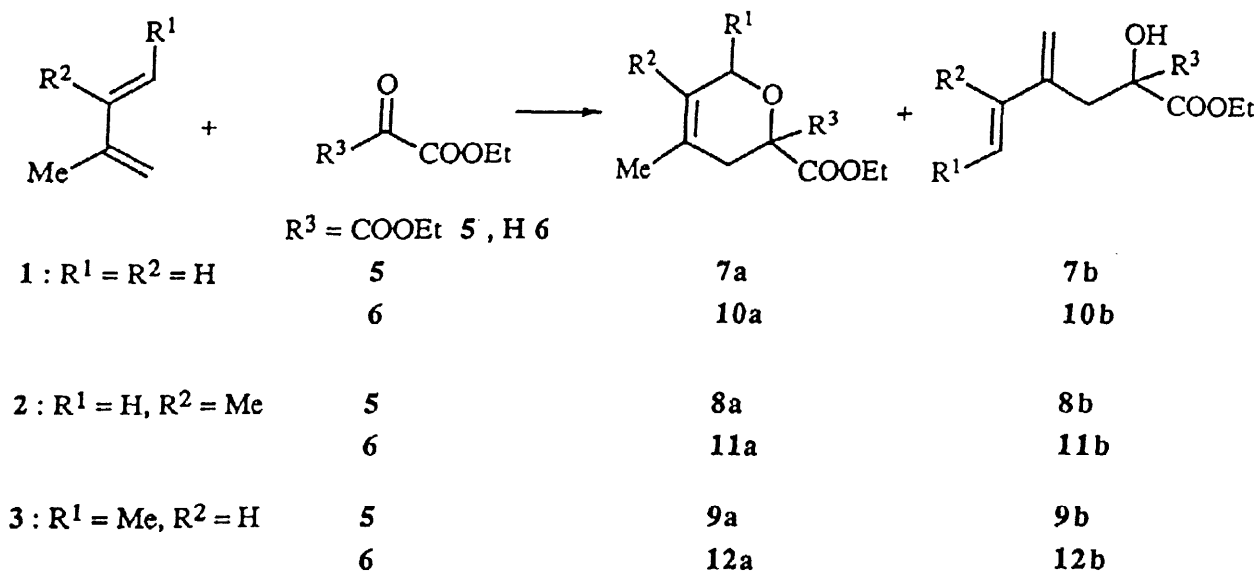
Among the activation methods of the Diels-Alder reaction, Lewis acid catalysis is certainly the most important.^{1,2} Recently, work on bismuth (III) derivatives,³ in particular by our laboratory, have demonstrated their catalytic activity as Lewis acids in several reactions such as acylation reactions (Friedel-Crafts,⁴ of enoxysilanes⁵ and of allylsilanes⁶), or cross-aldol and Michael reactions according to Mukaiyama⁷ and carbonyl-ene reaction.⁸ In our first examination of the Diels-Alder reaction, we showed the catalytic power of two Bi (III) derivatives, the chloride and the triflate, on the dienophilic activity of α -ethylenic aldehydes and ketones.⁹

The target of this study is to evaluate the catalytic activity of bismuth trichloride on the carbonyl-Diels-Alder reaction involving ethyl mesoxalate **5** and ethyl glyoxylate **6** as dienophiles. The reactivity of these two carbonyl dienophiles have been examined with four dienes, isoprene **1**, 2,3-dimethyl-1,3-butadiene **2**, 2-methyl-1,3-pentadiene **3** and 1,3-cyclohexadiene **4**.

Previously, most reactions with **5** have been carried out under elevated pressures and between 50°C and 180°C over several hours,¹⁰⁻¹⁶ sometimes in water.¹⁷ The activation by a Lewis acid has been little studied.^{13,18} In order to react with a diene, ethyl glyoxylate **6** always requires the presence of a catalyst, and when the diene structure allows it, the [4+2] cycloaddition product is often accompanied by the ene reaction product.¹⁹⁻²³ With ethyl mesoxalate **5** we reacted the dienes **1-3** (Table, Scheme 1), in chloroform at 20°C with **1**, and at 60°C with **2** and **3**, in the presence of 5% mol of BiCl₃. These experimental conditions led to the expected [4+2] adducts, the 2*H*-pyrans **7a-9a**, with average to very good yields. However, these reactions were not specific because of the competitive formation (15 to 25%) of the ene reaction product, **7b-9b**, respectively. The products **a** and **b** were separable by chromatography.²⁴ The ratios of the Diels-Alder/ene reaction adducts, constant during the reaction, are really kinetic ratios. This result is original insofar as, to our knowledge, the competitive ene reaction adducts have not ever been described as competitive for Diels-Alder reactions with **5**. On the other hand, BiCl₃ catalysis allows mild experimental

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conditions and, contrary to the AlCl_3 catalysis,¹³ without polymerization of diene. The overall yields were also higher. The formation of adducts **7a** and **9a**, isomerically pure, follows frontier orbital theory²⁵, and their structure was established from comparison with ^{13}C nmr data of 2*H*-pyrans.²⁶



Scheme 1

Table : BiCl_3 -catalyzed Diels-Alder reactions with ethyl mesoxalate **5** and ethyl glyoxylate **6** as dienophiles ^a

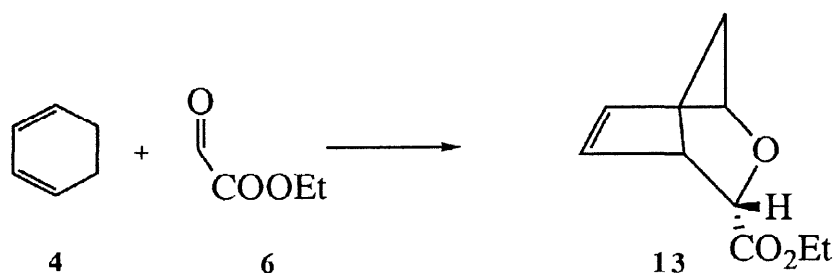
Entry	Diene ^b	Dienophile (conc.)	Temp. (°C)	Reaction time	Products	Yield (%) ^c
1	1	5 (1 M)	20	24 h	7a/7b (80/20)	54
2	2	5 (0.15 M)	60	3.5 h	8a/8b (85/15)	60
3	3	5 (0.15 M)	20	20 mn	9a/9b (85/15)	98
4	1	6 (0.3 M)	20	100 mn	10a/10b (65/35)	47
5	2	6 (0.15 M)	60	2 h	11a/11b (65/35)	75
6	3	6 (0.15 M)	60	30 mn	12a/12b (90/10)	96
7	4	6 (0.15 M)	60	1 h	13	50

^a 5% mol BiCl_3 ; solvent : chloroform ; ^b Excess of diene : 3 (entries 1,2,5,6,7) 4 (entry 3) or 5 equivalents (entry 4) with regard to the dienophile ; ^c Non optimised yield.

We reacted ethyl glyoxylate **6** with the dienes **1-4**, in experimental conditions comparable to those of preceding reactions (Table, Scheme 1 and 2), and obtained improved yields with regard to previous results in the literature.¹⁹⁻²² The dienes **1-3** gave a mixture of Diels-Alder **10a-12a** and of ene reaction **10b-12b** adducts, in which the former are the major products 3 (65 to 90%). The adduct **12a** was isolated in very good yield from **3**, after 30 min at 60°C (Table, entry 6), as a mixture of two diastereomers (*cis/trans* =

53/47).¹⁷ The reaction between **1** and **6** (rt; 100 min) led to only 47% yield of adducts **10** (Table, entry 4), but under the same conditions, a similar yield (43%) was obtained in presence of 10% of an Al-based catalyst after a much longer reaction time.²⁰ Like on previous studies,^{21,22} in the case of the 1,3-cyclohexadiene **4** we observed only the Diels-Alder product **13** (Scheme 2); the reaction was stereospecific (*endo*-**13**)²¹ and the yield was 50% after one hour at 60°C : 14h were required for a similar yield, at the same temperature, with Cu(OTf)₂.bis-oxazoline complex.²¹

The Lewis acidity of bismuth (III) compounds, in particular when the bismuth bears electronegative atoms,²⁷ have led to the identification of numerous complexes.²⁸ Among them, carbonyl complexes having an oxygen-bismuth bond are not very stable as a consequence of the softness (HSAB)²⁹ of the acidity of bismuth. However, an intramolecular complex in which the bismuth is coordinated to a carbonyl group was recently isolated.³⁰ Moreover, a BiCl₃-acyl chloride interaction has been identified in the Bi-catalyzed



Scheme 2

Friedel-Crafts acylation.^{4b,c} An attempt to visualize by ¹³C nmr a carbonyl-bismuth interaction between BiCl₃ and **5**, from a solution of these compounds in nitromethane-*d*₃, as in our previous study,^{4b} failed. Consequently, the electrophilic assistance in the Bi-catalyzed reactions involving carbonyl compounds, i.e., Mukaiyama-aldol and -Michael reactions,⁷ an amplification of the dienophilic activity of α -ethylenic aldehydes and ketones⁹, except acyl chlorides,^{4b,c} could not be shown.

In conclusion, these results account for the catalytic power of the bismuth (III) chloride in the hetero-Diels-Alder reactions involving carbonyl dienophiles, ethyl mesoxalate and ethyl glyoxylate. This catalyst turned out to be selective for the [4+2] cycloaddition but not chemospecific. Compared with previous results of the literature, BiCl₃ brings some advantages : its effectiveness allows one to lower notably the reaction temperature and to work in an open reactor; it is not very hygroscopic; in the described experimental conditions, it does not cause the polymerization of diene; finally, it is a commercial, low cost and non toxic³¹ compound.

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References and Notes

- (a) Carruthers, W. in *Cycloaddition Reactions in Organic Synthesis, Tetrahedron Org. Chem. Series*, Vol 8; Pergamon Press: Oxford, 1990, pp. 1-208; (b) March, J. *Advanced Organic Chemistry, Reactions, Mechanisms and Structure*; J. Wiley: New York, 1994, pp. 839-852.
- (a) Narasaka, K. *Synthesis* 1991, 1-11; (b) Kagan, H.; Riant, O. *Chem. Rev.* 1992, 92, 1007-1019; (c) Oh, T.; Reilly, M. *Org. Prep. Proc.* 1994, 26, 129-158; (d) Ishihara, K.; Yamamoto, H. *Adv. Catal. Proc.* 1995, 1, 29-59.
- Suzuki, H.; Ikegami, T.; Matano, Y. *Synthesis* 1997, 249-267 and references therein.
- (a) Dubac, J.; Labrouillère, M.; Laporterie, A.; Desmurs, J.R. *Eur. Pat. Appl.* 1996, EP 698,593 (*Chem. Abstr.* 1996, 124, 316758y); (b) Desmurs, J.R.; Labrouillère, M.; Dubac, J.; Laporterie, A.; Gaspard, H.; Metz, F. *Ind. Chem. Libr.* 1996, 8 (*The Roots of Organic Development*), 15-28; (c) Dubac, J.; Gaspard, H.; Labrouillère, M.; Laporterie, A.; Desmurs, J.R.; Le Roux, C. *PCT Int. Appl. WO 97 11,930 (Chem. Abstr.* 1997, 126, 317246h).
- Le Roux, C.; Mandrou, S.; Dubac, J. *J. Org. Chem.* 1996, 61, 3885-3887.
- Le Roux, C.; Dubac, J. *Organometallics* 1996, 15, 4646-4648.
- (a) Wada, M.; Takeichi, E.; Matsumoto, T. *Bull. Chem. Soc. Jpn.* 1991, 69, 990-994; (b) Le Roux, C.; Gaspard-Illoughmane, H.; Dubac, J. *J. Org. Chem.* 1993, 58, 1835-1839; (c) Le Roux, C.; Gaspard-Illoughmane, H.; Dubac, J. *Bull. Soc. Chim. Fr.* 1993, 130, 832-842; (d) Labrouillère, M. *Thesis*, Université Paul Sabatier, Toulouse 1995, n° 2133.
- Peidro, L.; Le Roux, C.; Laporterie, A.; Dubac, J. *J. Organomet. Chem.* 1966, 521, 397-399 and references therein.
- Garrigues, B.; Gonzaga, F.; Robert, H.; Dubac, J. *J. Org. Chem.* 1997, 62, 4880-4882.
- Achmatowicz, O.; Zamojski, A. *Roczniki Chem.* 1961, 35, 1251-1262.
- Boujouklian, R.; Ruden, R. A. *J. Org. Chem.* 1977, 42, 4095-4103.
- Achmatowicz, O.; Jurczak, J.; Pyrek, J.S. *Tetrahedron* 1976, 32, 2113-2116.
- Belanger, J.; Landry, N.L.; Pare, J.R.; Jankowski, K. *J. Org. Chem.* 1982, 47, 3649-3652.
- Abele, W.; Schmidt, R.R. *Tetrahedron Lett.* 1981, 22, 4807-4810.
- Potthoff, B.; Breitmaier, E. *Chem. Ber.* 1986, 119, 2059-2061.
- Schmidt, R.; Wagner, A. *Synthesis* 1981, 273-275.
- Grand, E. *Thèse*, Université Paris XI, Orsay, 1994, n° 3287, 124-127.
- Quimper, M.; Jankowski, K. *J. Chem. Soc., Chem. Commun.* 1987, 676-677.
- Klimova, E.I.; Treshchova, E.G.; Arbuzov, Y. *Zh. Org. Khim.* 1970, 6, 413-416.
- Graven, A.; Johannsen, M.; Jorgensen, K.A. *J. Chem. Soc., Chem. Commun.* 1996, 2373-2374.
- Johannsen, M.; Jorgensen, K.A. *J. Org. Chem.* 1995, 60, 5757-5762.
- Johannsen, M.; Jorgensen, K.A. *Tetrahedron* 1996, 52, 7321-7328.
- Qian, C.; Huang T. *Tetrahedron Lett.* 1997, 38, 6721-6724.
- Typical procedure:** A mixture of chloroform solution (0.15 or 1M) of dienophile and bismuth trichloride (5% mol) was agitated in a flask for 20 min. A chloroform solution of the diene (see table for equivalents) was added dropwise, and the reaction was kept under agitation during the time indicated in the table. The reaction mixture was quenched with 10 mL of a saturated sodium bicarbonate, and extracted with dichloromethane. The organic layers were combined, dried over sodium sulfate, and concentrated under reduced pressure. The crude product was analyzed according to previously described methods. The isomers **a** and **b** were separated by column chromatography (silica gel; eluent: hexane/ethyl acetate, 5:1, v:v). All compounds had ¹H NMR spectra identical to those previously reported. The new products were characterized by NMR. For example. **7a**: RMN ¹H: 5.35 (m, 1H), 4.30 (m, 6H), 2.46 (s, 2H), 1.66 (s, 3H), 1.16 (t, 6H). RMN ¹³C: 168.1, 129.5, 118.1, 79.7, 63.8, 61.9, 33.4, 22.8, 13.9. **7b**: RMN ¹H: 5.08 (m, 5H), 4.15 (m, 4H), 2.89 (s, 2H), 1.13 (t, 6H); RMN ¹³C: 169.9, 140.0, 138.9, 119.5, 114. 76.5, 62.3, 35.4, 13.8.
- Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; J. Wiley: New York, 1976, p.140-141.
- Eliel, E.L.; Monoharan, M.; Pietrusiewicz, K.M.; Hargrave, K.D. *Org. Magn. Res.* 1983, 21, 94-107.
- (a) Reese, A.L.; McMartin, K.; Miller, D.; Wickham, P.P. *J. Org. Chem.* 1973, 38, 764-768.
(b) Nakamura, E.; Shimada, J.; Kuwajima, J. *Organometallics* 1985, 4, 641-646.
- Lange, K.C.H.; Klapötke, T.M. in *The Chemistry of Arsenic, Antimony and Bismuth Compounds*; Patai, S., Ed.; J. Wiley: New York, 1994, pp. 315-366.
- (a) Pearson, R.G. *J. Am. Chem. Soc.* 1963, 85, 3533-3539; (b) Pearson, R.G.; *Science* 1966, 151, 172-177; (c) Parr, R.G.; Pearson, R.G. *J. Am. Chem. Soc.* 1983, 105, 7512-7516; (d) Pearson, R.G. *J. Chem. Educ.* 1987, 64, 561-567
- Murafuji, T.; Mutoh, T.; Satoh, K.; Tsunenari, K. *Organometallics* 1995, 14, 3848-3854.
- (a) Irwing-Sax, N.; Bewis, R.J. *Dangerous Properties of Industrial Materials*, Van Nostran Reinhold, 1989, pp. 283, 284, 522, 523; (b) Wormser, U.; Nir, I. in *The Chemistry of Arsenic, Antimony and Bismuth Compounds*; Patai, S., Ed.; J. Wiley: New York, 1994, pp.715-723.