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Lewis Acid-Promoted Generation of α-oxy-*o*-Quinodimethanes and Cycloaddition Reactions

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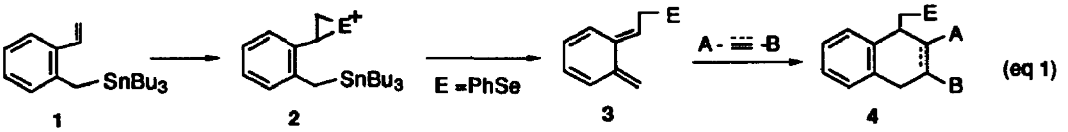
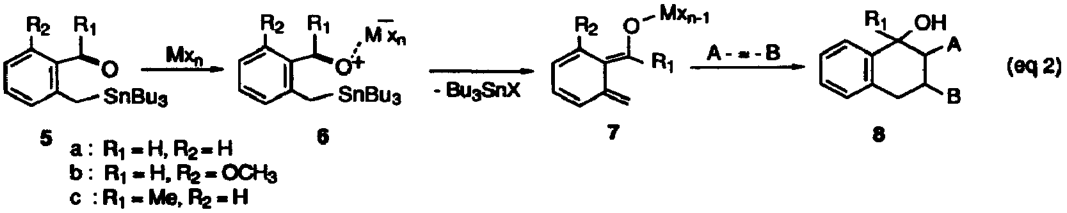
Abstract : *Treatment of stannyl aldehydes 5a, 5 b, and ketone 5c with $MgBr_2$ as the Lewis acid catalyst can initiate the internal cleavage reactions of carbon-tin σ bond leading to α-oxy-o-quinodimethanes, which can then undergo Diels - Alder cycloadditions.*

We recently reported that *o*-quinodimethane 3 generated *in situ* by addition of phenylseleno-phthalimide to *o*-vinyl benzyltributylstannane 1 in CH_2Cl_2 containing $ZnBr_2$(1.2 equiv) at 0° C could be trapped successfully as the Diels - Alder cycloaddition products 4 in good yields(eq. 1).[1]



(eq 1)

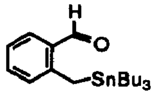
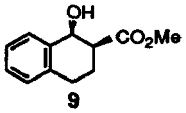
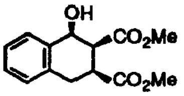
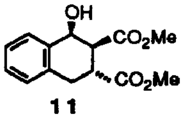
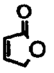
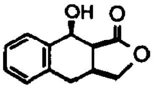
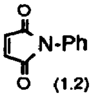
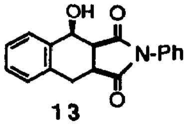
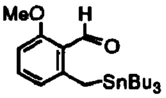
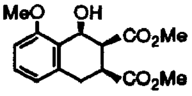
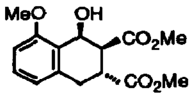
As an extension of this methodology, we next turned our attention to the carbonyl-initiated cleavage reactions of the carbon-tin σ bond[2,3] for the possible generation of α-oxy-*o*-quinodimethanes (eq. 2). It was envisaged that under appropriate Lewis acid catalyzed conditions the activated carbonyl would promote the internal carbon-tin bond cleavage reactions at low temperature(< rt) leading to α-oxy-*o*-quinodimethanes 7, which might then undergo Diels - Alder cycloaddition reactions with high regio- and stereoselectivities.[4]



(eq 2)

To test the feasibility of the sequences outlined in eq 2, we first examined the reactivity of stannyl aldehyde **5a**[5] toward dienophiles in the presence of Lewis acids. It was found that neither $ZnBr_2$ nor

Table 1. $MgBr_2$- promoted Cycloadditions of 5a and 5b with Dienophiles[a]

Entry	Stannyl aldehydes	Dienophile (Molar equiv)	Time	Endo product	Ratio[b] endo : exo	Yield[c] %
1	 5a	$CH_2 = CHCO_2Me$ (3)	1h	 9	>20 :1	58
2[d,e]	5a	cis $MeO_2CCH = CHCO_2Me$ (1.4)	1.5h	 10	10 : 1	76
3[d]	5a	trans $MeO_2CCH = CHCO_2Me$ (1.4)	2h	 11	3.3 : 1 (5.3 : 1)	66 (64)[f]
4[d,g]	5a	 (1.5)	2h	 12	>50 : 1	64
5[g]	5a	 (1.2)	1h	 13	1.2 : 1	77
6[e]	 5b	cis $MeO_2CCH = CHCO_2Me$ (1.2)	1.5h	 14	7.3 : 1	70
7	5b	trans $MeO_2CCH = CHCO_2Me$ (1.2)	2h	 15	1.6 : 1	67

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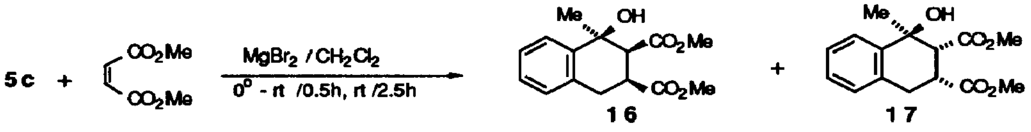
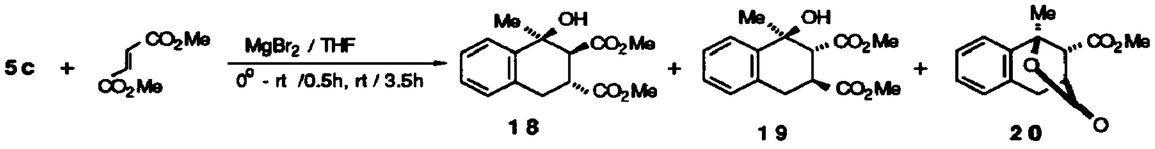
[a] Unless otherwise noted, reactions were carried out on a 0.5 mmol scale at 0°C in CH_2Cl_2 with 1.2 equiv of $MgBr_2$. [b] Isomeric ratios (endo vs exo) were determined on the crude reaction mixture by 300MHz ^1H- NMR and /or isolation of pure isomers. [c] Isolated combined yields after flash column chromatography. [d] Spectral data of **10**(exo),**11**(endo) and **11**(exo) are given in supplementary material of ref. 7a. [e] Ref. 8 [f] THF was used as the solvent. [g] Spectral data of **12** and **13** are given in ref. 9a and 9b, respectively.

$BF_3 \cdot Et_2O$ could promote the reaction of **5a** with methyl acrylate to give adducts arising from cycloaddition. However, exposure of 0. 5 M solution of **5a** in CH_2Cl_2 containing methyl acrylate(3 equiv) to anhydrous $MgBr_2$ (1.2 equiv) at 0°C led to rapid consumption of the starting material giving rise, after aqueous work-up, to exclusively 1, 2 - cis, endo adduct **9** in 58 % yield(Table 1, entry 1). On the basis of these results, we have studied the $MgBr_2$-promoted reactions of **5** with several dienophiles. As summarized in Table 1, the $MgBr_2$- prompted cycloaddition reactions of stannyl aldehydes **5a** and **5b**[5] with dienophiles proceed rapidly at 0°C to afford good yields of the Diels-Alder adducts.[6] In the cycloaddition reactions with dimethyl maleate (entries 2 and 6), high levels of endo vs exo stereoselection were obtained. It is interesting to note that the observed endo stereoselectivity (10 : 1) in entry 2 is noticeably superior to those obtained in the published methods utilizing benzocyclobutanol or its lithiated alkoxide as α-oxy-*o*-quinodimethane precursor.[7a] In contrast, analogous reactions with dimethyl fumarate (entries 3 and 7) were somewhat less stereoselective than the proceeding cases. However, when the reaction was carried out in THF at the lower temperature(-40° - 0°C), the endo to exo stereoselectivity could be enhanced to 5.2 : 1(entry 3). In a sharp contrast to the high degree of endo selectivity(> 50 :1) obtained in the reaction of **5a** with γ - cronolactone(entry 4), virtually no stereoselectivity(1.2 : 1) was seen in the reaction with N-phenyl maleimide(entry 5). This result was surprising since cyclic dienophiles usually added to *o* -quinodimethanes with high endo stereoselectivities.[1,4] The origin of the low selectivity observed in this instance is not yet clear.

In order to further increase the utility of the present method, we next examined the cycloaddition behavior of stannyl ketone **5c** in the presence of $MgBr_2$. To our delight, **5c** underwent clean cycloaddition with dimethyl maleate(1.2 equiv) in CH_2Cl_2 containing $MgBr_2$(1.2 eqiv) at ambient temperature to produce adducts **16** and **17** as a 9 : 1 mixture in 76 % combined yield, in favor of the endo product **16**.[8] An analogous reaction with dimethyl fumarate in THF solvent[10] under otherwise similar conditions gave a mixture of endo adduct **18** (43%), exo adduct **19** and its corresponding γ - lactone **20**(**19**+ **20**, 13%).

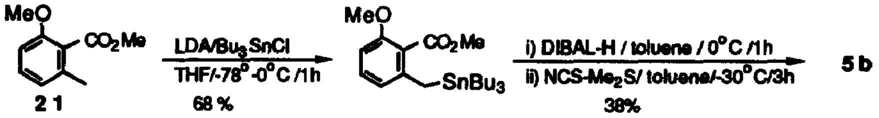




In summary, we have shown that anhydrous $MgBr_2$ can effectively promote to the conversion of **5** to α-oxy - *o* -quinodimethanes **7**, which subsequently undergo Diels-Alder cycloadditions. The mild reaction conditions coupled with the operational simplicity make this method attractive and should find wide applications in the synthesis of polycyclic structures.

REFERENCES AND NOTES

1. Woo, S. H. *Tetrahedron Lett*. **1993**, *34*, 7587-7590.
2. For recent examples of electrophile-mediated C -Sn cleavage reactions leading to carbocycles, see (a) Macdonald T. L.; Delahunty, C. M. ; Mead, K. ; O'Dell, D. E. *Tetrahedron lett*. **1989**, *30*, 1473-1476. (b) Herndon, J.W. ; Harp, J. J. *Tetrahedron lett*. **1992**, *33*, 6243 - 6246 and references cited therein.
3. For the first example to utilize the C-Sn bond as a latent nucleophile for the generation of *o* -quinodimethanes, see Sano, H. ; Ohtsuka, H.; Migita, T. *J. Am. Chem. Soc*. **1988**, *110*, 2014-2015.
4. For a recent review on *o* - quinodimethanes, see (a) Charlton, J. L. ; Alauddin, M. M. *Tetrahedron*, **1987**, *43*, 2873-2889. (b) Martin, N. :Seoane, c.; Hanack, M. *Org. Pre. Proc. Int.* **1991**, *23*, 237-272.
5. The starting aldehyde **5a**[1] and ketone **5c** were prepared in respective 87 % and 76 % yield from the known corresponding alcohols [3] by oxidation (NCS-Me_2S / Et_3N / toluene / -30°C / 3h) using the procedure of Corey, E.J. ; Kim. C. U. *J. Am. Chem. Soc*. **1972**, *94*, 7586-7587. **5b** was prepared from methyl 2-methoxy-6-methyl benzoate **21** in three steps, as shown below. For discussions on carbanion chemistry of *o* -toluate including **21**, see Hauser, F. M. ; Rhee, R. P. ; Prasanna, S.; Weinreb, S.M. ; Dodd, J. H. *Synthesis*, **1980**, 72-74.



6. A typical experimental was as follows : To a stirred solution of **5a** (204 mg, 0.5 mmol) and dimethyl maleate (100 mg, 0.7 mmol) in dry methylene chloride(1 ml) under argon at 0° C was added anhydrous magnesium bromide (110 mg, 0.6 mmol). After stirring at 0°C for 1.5h, the reaction mixture was poured into an ice-cold water(5 ml), extracted with ethyl acetate(10 ml x 3), dried ($MgSO_4$), and concentrated. The residue obtained was then dissolved in acetonitrile(20ml) and washed with hexane (10 ml, x5) to remove organotin products. The acetonitrile layer was concentrated under reduced pressure and the residue was purified by flash chromatography on silica gel eluting with hexane / ethyl acetate (2 /1) to give endo adduct **10** (91mg) and its exo isomer[7a] (9mg) in a 76 % combined yield . **10** : ^{1}H-NMR(300MHz, $CDCl_3$) ; δ 3.05-3.40(m, 4H), 3.71(s, 3H), 3.76 (s, 3H), 4.40 (d, 1H, J = 9.8Hz), 5.03(dd, 1H, J = 9.8Hz, J = 5.0 Hz), 7.09 -7.58 (m, 4H). ^{13}C-NMR (75 MHz, $CDCl_3$) ; δ 30.07, 38.70, 47.12, 52.15, 52.30, 67.41, 126.84, 127.93, 128.47, 128.89, 132.48, 137.12, 172.65, 174.50.
7. (a)Choy, W. ; Yang, H. *J. Org. Chem.* 1988, 53, 5796 - 5798. For related reactions, see (b)Kündig, E. P. ; Bernardinelli, G. ; Leresche, J. *J. Chem. Soc. Chem. Commun*. 1991, 1713 -1715. (c) Wey, H. G. ; Butenschön, H. *Angew. Chem. Int. Ed. Engl.* 1991, *30*, 880 - 881.
8. The indicated endo adducts **10**, **14**, and **16** can be heated overnight in refluxing xylenes to produce their respective γ - lactones.
9. (a)Arnold, B. J. ; Mellows, S. M. ; Sammes, P. G. ; Wallace, T. W. *J. Chem. Soc., Perkin Trans. I*, **1974**, 401-409.(b) Arnold, B. J. ; Sammes, P. G.; Wallace, T. W. *J. Chem. Soc., Perkin Trans. I*, **1974**, 409 -414.
10. It might be mentioned that when CH_2Cl_2 was used as the solvent, the reaction became sluggish and failed to produce any detectable amounts of the expected adducts. Unreacted starting compound **7** and methyl acetophenone derived from protodestannylation were obtained. This solvent effect was surprising and would imply that the cycloaddition reaction proceed via stepwise, ionic pathway rather than a concerted process. For discussions on the solvents effects on rates and stereoselectivity in the Diels-Alder cycloadditions, see a recent review of Pindur, U. ; Lutz, G. ; Otto, C. *Chem. Rev.* **1993**, *93*, 741 -761.

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