

information about the topology of the potential surface and show promise as a means of investigating other fundamental reactions.

**Acknowledgment.** We are grateful to the National Science Foundation for support of this research. We thank Brian Wladkowski for advice and help with the RRKM calculations.

**Registry No.** ClCO<sub>2</sub>CH<sub>3</sub>, 79-22-1; Cl<sup>-</sup>, 16887-00-6; CF<sub>3</sub>CO<sub>2</sub>CH<sub>3</sub>, 431-47-0.

## Stereoselective Chelation-Controlled Reduction of $\alpha$ -Iodo- $\beta$ -alkoxy Esters under Radical Conditions<sup>1</sup>

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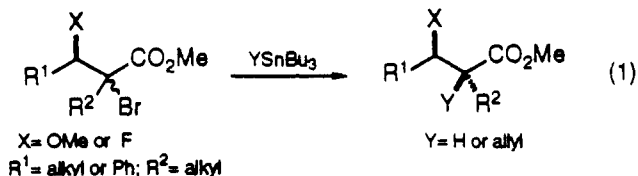
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Received August 1, 1991

The application of free-radical reactions in organic synthesis has grown enormously during the past decade providing a wealth of useful new chemistry.<sup>2</sup> However, relatively few reports have addressed the problem of stereocontrol in reactions involving acyclic radicals. Very recently it has been shown that chirality transfer can be achieved successfully using chiral auxiliaries<sup>3</sup> or stereogenic centers adjacent to the radical center.<sup>4,5</sup> In this communication we describe an alternative solution to the problem of stereocontrol in acyclic molecules wherein chelation-controlled reductions are performed under radical conditions.

Previously, we reported that the radical-mediated reduction<sup>5b</sup> or allylation<sup>5c</sup> of acyclic  $\beta$ -methoxy- $\alpha$ -halo or  $\beta$ -fluoro- $\alpha$ -halo esters proceeds with good to excellent stereoselectivity (eq 1). To



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(1) Presented at the 74th Canadian Chemical Conference and Exhibition, Hamilton, Ontario, Canada, June 1991.

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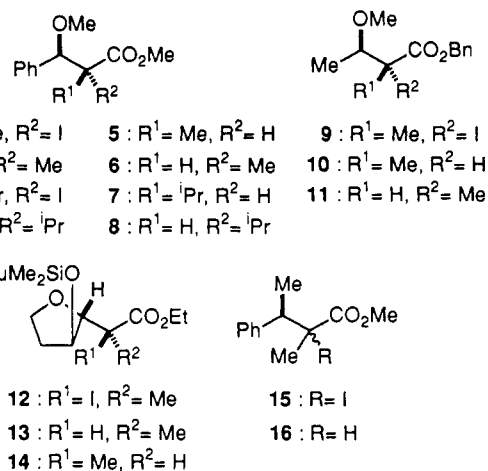
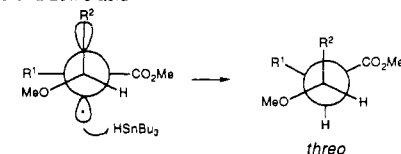


Figure 1.

### Scheme I

a. In absence of a Lewis acid



b. In presence of a Lewis acid

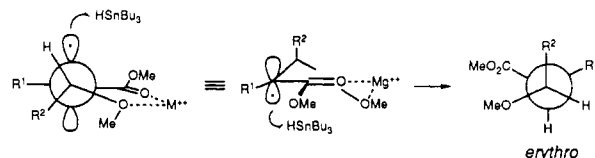


Table I. Reduction of Iodoester 1 with Bu<sub>3</sub>SnH in the Presence of Various Lewis Acids

entry	Lewis acid	equiv	ratio <sup>a</sup> (erythro:threo)	yield, %
1			1: >25	90
2	MgI <sub>2</sub>	1.0	>25:1	78
3	MgI <sub>2</sub>	0.25	25:1	71
4	MgBr <sub>2</sub> ·OEt <sub>2</sub>	1.0	>25:1	84
5	MgBr <sub>2</sub> ·OEt <sub>2</sub>	0.25	>25:1	81
6	AlCl <sub>3</sub>	1.0	>25:1 <sup>b</sup>	75
7	AlCl <sub>3</sub>	0.24	1:1.8	

<sup>a</sup> Ratios determined by <sup>1</sup>H NMR spectroscopy. <sup>b</sup> Threo diastereomer could not be detected by <sup>1</sup>H NMR spectroscopy.

account for this stereochemical outcome we proposed a transition state as depicted in Scheme Ia.<sup>5b</sup> Consideration of this model led to the hypothesis that a bidentate Lewis acid could alter the structure of the transition state thus changing the stereochemical outcome of the reaction. As shown in Scheme Ib, chelation of the carbonyl and methoxy moieties to a Lewis acid forces the molecule into a conformation which exposes the top face of the radical  $\pi$  system (Newman projection) to hydrogen atom delivery and thus provides access to the erythro manifold.<sup>6</sup>

In order to test this hypothesis, iodo ester 1<sup>7</sup> was treated with Bu<sub>3</sub>SnH in the presence of various Lewis acids. As shown in Table I, excellent erythro selectivities were observed when MgI<sub>2</sub>, MgBr<sub>2</sub>·Et<sub>2</sub>O, or AlCl<sub>3</sub> were employed (entries 2, 4, and 6).<sup>8-10</sup>

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(9) SnCl<sub>4</sub> and EtAlCl<sub>2</sub> gave only moderate amounts of erythro products. The use of ZnCl<sub>2</sub>, ZnI<sub>2</sub>, MgCl<sub>2</sub>, or BF<sub>3</sub>·Et<sub>2</sub>O gave predominantly the threo isomer.

Table II. Reduction of  $\alpha$ -Iodo Esters with  $\text{Bu}_3\text{SnH}$ 

entry	iodide	con- ditions <sup>a</sup>	ratio <sup>b</sup> (erythro:threo)	products (erythro:threo)	yield, %
1	1	A	>25:1	5:6	78 <sup>c</sup>
2	1	B	1:>25	5:6	86 <sup>d</sup>
3	2	A	1:4	5:6	61 <sup>e</sup>
4	2	B	1:>25	5:6	85 <sup>d</sup>
5	3	A	>25:1	7:8	79 <sup>c</sup>
6	3	B	1:24	7:8	87 <sup>d</sup>
7	4	A	1:2.3	7:8	76 <sup>e</sup>
8	9	A	5:1	10:11	82 <sup>e</sup>
9	9	B	1:4	10:11	80 <sup>e</sup>
10	12	A	10:1	13:14 <sup>f</sup>	53 <sup>c</sup>
11	12	B	1:>25	13:14 <sup>f</sup>	93 <sup>d</sup>
12	15	A	1:2.2	16 <sup>g</sup>	88 <sup>e</sup>
13	15	B	1:2.3	16 <sup>g</sup>	89 <sup>e</sup>

<sup>a</sup>A:  $\text{HSnBu}_3$  (2 equiv),  $\text{MgI}_2$  (2 equiv),  $\text{CH}_2\text{Cl}_2$  (0.04–0.05 M),  $-50^\circ\text{C}$ , 1 h, then  $0^\circ\text{C}$ , 30 min. B:  $\text{HSnBu}_3$  (2 equiv) catalytic AIBN, toluene (0.1 M),  $-78^\circ\text{C}$ ,  $h\nu$  (sunlamp, 275 W). <sup>b</sup>Ratios determined by  $^1\text{H}$  NMR spectroscopy unless otherwise indicated. <sup>c</sup>Isolated yield of pure erythro isomer. <sup>d</sup>Isolated yield of pure threo isomer. <sup>e</sup>Total isolated yield. <sup>f</sup>Ratio determined by gas chromatographic analysis. <sup>g</sup>Relative stereochemistry not determined.

Interestingly, the use of catalytic amounts of  $\text{MgI}_2$  or  $\text{MgBr}_2\cdot\text{Et}_2\text{O}$  resulted in no loss of diastereoselection (entries 3 and 5) while  $\text{AlCl}_3$  provides good ratios only if a full equivalent is added (entry 7). In addition, no radical initiator is required for these reactions to proceed, the initiation step probably occurring via a single electron transfer process between  $\text{Bu}_3\text{SnH}$  and the electron-deficient chelate.<sup>11</sup>

Contrary to many radical reductions, the configuration of the substrate iodide has a significant effect on the stereochemical outcome of the reaction (Table II). Iodides in which the alkoxy group and iodo moiety are anti (1, 3, 9, 12) show a marked preference for producing erythro products when  $\text{MgI}_2$  is present while compounds in which the alkoxy and iodo groups are syn (2, 4)<sup>12</sup> show a modest preference for the threo isomer in the presence of  $\text{MgI}_2$ . The syn and anti iodides react identically in the absence of  $\text{MgI}_2$  producing selectively the threo products (entries 2 and 4).<sup>5b</sup> One could rationalize these results by suggesting that the chelated form of the syn iodide is less reactive than the anti iodide in the initial phase of the reaction (C–I breakage) due to developing  $\text{A}_{1,2}$  strain in the transition state. In the case of syn iodides, the unchelated pathway would therefore be more energetically favored.

The described chemistry provides a novel approach to control of stereochemistry in acyclic radical reactions<sup>13</sup> and is of potential synthetic utility due to its mildness and the ready availability of the starting materials. We are currently investigating the mechanistic aspects of this transformation, the results of which will be published in a full account of this work.

**Acknowledgment.** A Natural Sciences and Engineering Research Council of Canada (N.S.E.R.C.) Industrial Research Fellowship (J.R.) and a University Undergraduate Research Award (G.H.) are gratefully acknowledged. The authors thank Dr. W. Ogilvie for assistance during the preparation of this manuscript.

**Supplementary Material Available:** Experimental procedures and spectral data ( $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, IR, MS, analysis and/or HRMS) for compounds 1–16 (11 pages). Ordering information is given on any current masthead page.

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(12) Obtained by isomerization of 1 ( $\text{LiI}\cdot 3\text{H}_2\text{O}$ , THF, reflux, 16 h).

(13) Although the presence of a free radical in this reaction has not been firmly established, one will note that the inclusion of deuterated methanol in the reaction medium could not compete with  $\text{Bu}_3\text{SnH}$  as a hydrogen donor, indicating that a radical is probably involved in the reaction.

## Photoreaction of Meldrum's Diazo in Poly(methyl methacrylate) Matrices

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Received May 22, 1991

Revised Manuscript Received October 18, 1991

Most photochemical reactions are carried out in solution. In the liquid phase, excited molecules normally are able to explore a variety of accessible conformations before reacting. In the solid state, much of this motion is suppressed. In recent years there has been an extensive effort, nicely reviewed by Scheffer,<sup>1</sup> to study photochemical reactions in organic crystals, where the molecular conformation prior to excitation is the same for each molecule. Very special features appear in the photoreaction of organic molecules dissolved in rigid polymer films. This is a field pioneered by Smets and his group in Belgium<sup>2</sup> and reviewed recently.<sup>3,4</sup> The fundamental characteristic of photoreactions in glassy polymer films is their sensitivity to the distribution of free volume in the film: Below the glass transition temperature ( $T_g$ ), large-scale motion of the polymer is suppressed. As a consequence, if a reaction of a guest molecule involves a change in conformation, the reaction will occur faster in molecules adjacent to sites of substantial free volume, and the reaction rate and quantum efficiency ( $\Phi_r$ ) will decrease as the reaction proceeds. This is clearly the case with a wide variety of photochromic molecules studied by Smets and others, and this principle has been employed by Horie<sup>5a</sup> and by Torkelson<sup>5b</sup> as a means of mapping out the free volume distribution in amorphous polymer films below  $T_g$ . It is not surprising that most photoreactions have substantially lower  $\Phi_r$  values in rigid films than in solution. There are a few rare examples of reactions that have higher  $\Phi_r$  values in polymer films, one set involving proton tautomerism in benzoylacetonilides,<sup>6</sup> held in the proper geometry by intramolecular hydrogen bonding, and one involving ring closure of an imine oxide to an oxazirine.<sup>7</sup>

This paper describes the photochemistry of Meldrum's diazo (1) in poly(methyl methacrylate) (PMMA) films at  $22^\circ\text{C}$ . 1 is of interest to organic chemists because of the question of whether its Wolff rearrangement involves the singlet carbene as a discrete intermediate.<sup>8,10</sup> 1 and its derivatives are also of interest in the microelectronic area since they display many of the ideal characteristics ( $\lambda_{\text{max}} \approx 250$  nm, transparent photoproducts) of photoactive additives for deep UV photoresists. Effective resists have been reported for 1 in Novolac films,<sup>11</sup> and irradiation of 1 in PMMA films causes those films to dissolve much faster upon

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