

## Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:

<http://www.tandfonline.com/loi/lcyc20>

### MAGNESIUM IN METHANOL MEDIATED DEOXYGENATION OF THE CYCLIC THIONOCARBONATES OF AROMATIC 2,3-DIHYDROXY ESTERS

Ho Sik Rho <sup>a</sup> & Byoung-Seob Ko <sup>b</sup>

<sup>a</sup> Department of Applied Skin Biology Institute , Pacific Corporation, 314-1, Bora-ri, Kiheung-eup, Yongin-Si, Kyounggi-do, 449-900, South Korea

<sup>b</sup> Institute of Oriental Medicine , Chongdam-dong, Kangnam-ku, Seoul, 135-100, South Korea

Published online: 16 Aug 2006.

To cite this article: Ho Sik Rho & Byoung-Seob Ko (2001) MAGNESIUM IN METHANOL MEDIATED DEOXYGENATION OF THE CYCLIC THIONOCARBONATES OF AROMATIC 2,3-DIHYDROXY ESTERS, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 31:2, 283-288, DOI: [10.1081/SCC-100000211](https://doi.org/10.1081/SCC-100000211)

To link to this article: <http://dx.doi.org/10.1081/SCC-100000211>

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at <http://www.tandfonline.com/page/terms-and-conditions>

SYNTHETIC COMMUNICATIONS, 31(2), 283–288 (2001)

## MAGNESIUM IN METHANOL MEDIATED DEOXYGENATION OF THE CYCLIC THIONOCARBONATES OF AROMATIC 2,3-DIHYDROXY ESTERS

Ho Sik Rho,<sup>1,\*</sup> and Byoung-Seob Ko<sup>2</sup>

<sup>1</sup>Department of Applied Skin Biology Institute, Pacific  
Corporation, 314-1, Bora-ri, Kiheung-eup, Yongin-Si,  
Kyounggi-do 449-900, South Korea

<sup>2</sup>Institute of Oriental Medicine, Chongdam-dong,  
Kangnam-ku, Seoul 135-100, South Korea

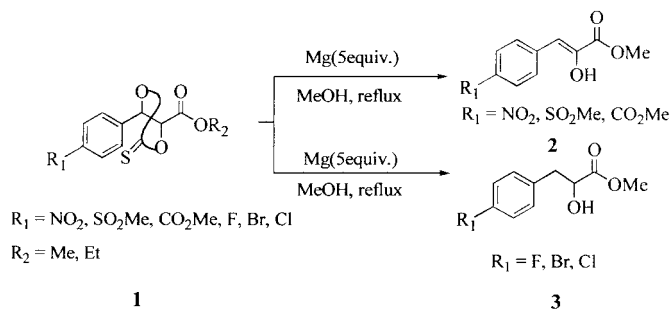
### ABSTRACT

The cyclic thionocarbonates of aromatic 2,3-dihydroxy esters, which have an electron-withdrawing group, undergo deoxygenation with magnesium in methanol to form  $\alpha$ -keto esters or  $\alpha$ -hydroxy esters, depending on the type of electron-withdrawing group.

$\alpha$ -Hydroxy ester functionality is frequently found in natural products and is valuable as a synthetic intermediate (1–3). They are usually prepared by the hydrolysis of  $\alpha$ -halo esters (4), rearrangement of  $\alpha$ -keto acetals (5), oxidation of ketene silyl acetals (6), reduction of  $\alpha$ -keto esters (7,8), ring opening of epoxy esters, and subsequent reduction of the resulting iodohydrins (9,10). Recently, we have reported that the cyclic thionocarbonates of 2,3-dihydroxy esters are good

---

\* To whom correspondence should be addressed. E-mail: thiocar@channeli.net



Scheme 1.

precursors for  $\alpha$ -hydroxy esters *via* regioselective deoxygenation process induced by magnesium in methanol (11). Here, we wish to report deoxygenation of the cyclic thionocarbonates of aromatic 2,3-dihydroxy esters that have an electron-withdrawing substituent (Scheme 1).

The results of deoxygenation of cyclic thionocarbonates are summarized in Table 1. The diols were transformed to the cyclic thionocarbonates by treating with thiophosgene. The *para* nitro substituted cyclic thionocarbonates **1a** reacted with magnesium (5 equiv.) in refluxing dry methanol for 30 min to afford methyl (2*Z*)-2-hydroxy-3-(4-nitrophenyl) prop-2-enoate (**2a**) (19,20) in 75% yield (entry 1 in Table 1). This unexpected conversion is due to the presence of an electron-withdrawing substituent on the aromatic ring. A plausible mechanism for this conversion is outlined in Figure 1.

The deoxygenation occurs exclusively at the  $\beta$ -position of the carbonyl group (8). The chelation of the magnesium cation has an effect on the selectivity of deoxygenation. Electron-withdrawing substituents destabilize the deoxygenated radical intermediate at the benzylic position. The radical intermediate is subsequently converted into the enol form by abstraction of  $\alpha$ -hydrogen. The destabilizing effect of the nitro group is the key factor to yield the  $\alpha$ -keto ester product. The enol structure was established by 300 MHz  $^1H$  NMR spectroscopy. For the methyl sulfone-substituted cyclic thionocarbonate **1b** and **1c** under the same conditions,  $\alpha$ -keto ester **2b** was obtained in 81% and 78% yields as the sole

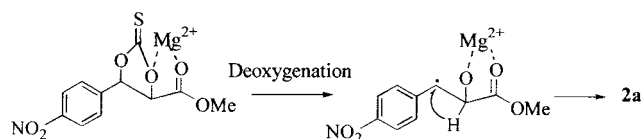
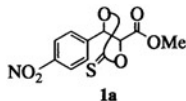
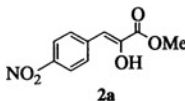
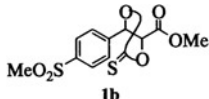
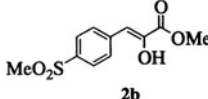
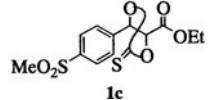
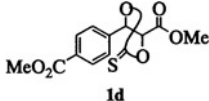
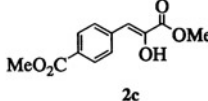
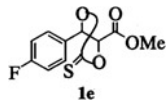
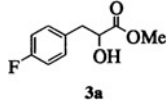
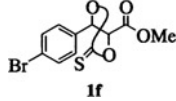
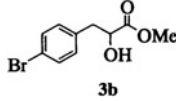
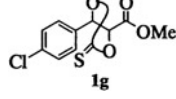
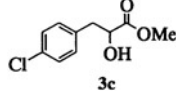


Figure 1.



**Table 1.** Magnesium in Methanol Induced Deoxygenation of the Cyclic Thionocarbonate of Aromatic 2,3-dihydroxy Esters<sup>a</sup>

Entry	Substrate	Time (min)	Product	Yield (%) <sup>b</sup>
1	 <b>1a</b>	30	 <b>2a</b>	75
2	 <b>1b</b>	35	 <b>2b</b>	81
3	 <b>1c</b>	40	<b>2b</b>	78
4	 <b>1d</b>	45	 <b>2c</b>	65
5	 <b>1e</b>	25	 <b>3a</b>	72
6	 <b>1f</b>	30	 <b>3b</b>	69
7	 <b>1g</b>	30	 <b>3c</b>	70

<sup>a</sup>All the reactions were run with magnesium (5 equiv.) in refluxing dry MeOH.

<sup>b</sup>The yields are for isolated compounds.

product (entry 2 and 3). The ethyl ester was transformed into the methyl ester by transesterification. In the case of ester-substituted compound **1d**,  $\alpha$ -keto ester **2c** was obtained together with a trace amount of  $\alpha$ -hydroxy ester (entry 4). However, we could not obtain pure product.

In contrast to the above cases, when the fluorosubstituted cyclic thionocarbonate **1e** was reacted with magnesium in methanol, methyl 2-hydroxy-3-(4-fluorophenyl) propanoate **3a** was obtained in 72% yield (entry 5). This result apparently indicates that the fluoro group does not destabilize the radical intermediate. The protonation of the radical intermediate must be faster than elimination in this case. The bromo-substituted cyclic thionocarbonate **1f** was also used to



prepare  $\alpha$ -hydroxy ester **3b** (entry 6). Finally, the chloro-substituted cyclic thionocarbonate **1g** with magnesium in methanol produced  $\alpha$ -hydroxy ester **3c** in 70% yield without formation of  $\alpha$ -keto ester (entry 7). Deoxygenation did not occur when magnesium in absolute ethanol was used. Anhydrous reaction conditions are important to reduce the formation of deprotected diol as side product.

In summary,  $\alpha$ -keto esters or  $\alpha$ -hydroxy esters were synthesized by magnesium in methanol-induced deoxygenation of the cyclic thionocarbonates of aromatic 2,3-dihydroxy esters containing an electron-withdrawing substituent.

## EXPERIMENTAL

### Typical Procedure

#### Methyl (2Z)-2-hydroxy-3-(4-nitrophenyl) Prop-2-enoate (2a)

To a stirred solution of the cyclic thionocarbonate **1a** (200 mg, 0.70 mmol) in dry MeOH (10 mL) under nitrogen atmosphere was added magnesium turning (85 mg, 3.53 mmol) and the reaction mixture was heated at reflux for 30 min. To the gray solution was added diethyl ether (30 mL) and the whole mixture was filtered through a celite pad and concentrated *in vacuo*. The crude product was purified by SiO<sub>2</sub> column chromatography (EtOAc/hexanes 1 : 1,  $R_f$  = 0.55) to give **2a** (118 mg, 75%). Mp 150°–151°C. IR (neat) 3451, 3010, 1732 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  8.21 (d, 2H,  $J$  = 9.6 Hz), 7.89 (d, 2H,  $J$  = 8.7 Hz), 6.81 (s, 1H), 6.55 (s, 1H), 3.97 (s, 3H). MS (m/e) 223 (M<sup>+</sup>), 163 (base peak), 136. Anal. calcd for C<sub>10</sub>H<sub>9</sub>O<sub>5</sub>N: C, 53.82; H, 4.06; N, 6.27. Found: C, 53.75; H, 3.99; N, 6.23.

#### Methyl (2Z)-2-hydroxy-3-[4-(methylsulfonyl)phenyl] Prop-2-enoate (2b)

TLC, SiO<sub>2</sub>, EtOAc/hexanes 1 : 1,  $R_f$  = 0.27. Mp 157°–158°C. IR (neat) 3453, 3011, 1730 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  7.92 (s, 4H), 6.73 (s, 1H), 6.54 (s, 1H), 3.96 (s, 3H), 3.06 (s, 3H). MS (m/e) 256 (M<sup>+</sup>), 196, 169, 107 (base peak). Anal. calcd for C<sub>11</sub>H<sub>12</sub>O<sub>5</sub>S: C, 51.55; H, 4.72; S, 12.51. Found: C, 51.47; H, 4.78; S, 12.46.

#### Methyl (2Z)-2-hydroxy-3-[4-(methoxycarbonyl)phenyl] Prop-2-enoate (2c)

TLC, SiO<sub>2</sub>, EtOAc/hexanes 1 : 1,  $R_f$  = 0.60. Mp 117–119°C. IR (neat) 3450, 3015, 1733 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  8.03 (d, 2H,  $J$  = 8.4 Hz), 7.81



## AROMATIC 2,3-DIHYDROXY ESTERS

287

(d, 2H,  $J = 8.4$  Hz), 6.64 (s, 1H), 6.54 (s, 1H), 3.93 (s, 3H), 3.91 (s, 3H). MS (m/e) 236 ( $M^+$ ), 176 (base peak), 149. Anal. calcd for  $C_{12}H_{12}O_5$ : C, 60.01; H, 5.12. Found: C, 59.94; H, 5.10.

### Methyl 2-hydroxy-(4-fluorophenyl) Propanoate (3a)

TLC,  $SiO_2$ , EtOAc/hexanes 1:1,  $R_f = 0.50$ . IR (neat) 3451, 3010, 1732  $cm^{-1}$ .  $^1H$  NMR ( $CDCl_3$ , 300 MHz)  $\delta$  7.26 (m, 2H), 7.08 (m, 2H), 4.42 (m, 1H), 3.77 (s, 3H), 3.12 (dd, 1H,  $J = 13.8, 4.2$  Hz), 2.92 (dd, 1H,  $J = 13.8, 8.1$  Hz), 2.76 (bs, 1H). MS (m/e) 198 ( $M^+$ ), 180, 109 (base peak). Anal. calcd for  $C_{10}H_{11}O_3F$ : C, 66.60; H, 5.59. Found: C, 66.71; H, 5.67.

### Methyl 2-hydroxy-(4-bromophenyl) Propanoate (3b)

TLC,  $SiO_2$ , EtOAc/hexanes 1:1,  $R_f = 0.52$ . IR (neat) 3450, 3015, 1733  $cm^{-1}$ .  $^1H$  NMR ( $CDCl_3$ , 300 MHz)  $\delta$  7.41 (d, 2H,  $J = 8.1$  Hz), 7.08 (d, 2H,  $J = 8.1$  Hz), 4.43 (m, 1H), 3.77 (s, 3H), 3.01 (dd, 1H,  $J = 13.8, 4.2$  Hz), 2.89 (dd, 1H,  $J = 13.8, 6.9$  Hz), 2.73 (bs, 1H). MS (m/e) 261 ( $M^{2+}$ ), 259 ( $M^+$ ), 241, 170 (base peak). Anal. calcd for  $C_{10}H_{11}O_3Br$ : C, 46.35; H, 4.28. Found: C, 46.20; H, 4.30.

### Methyl 2-hydroxy-(4-chlorophenyl) Propanoate (3c)

TLC,  $SiO_2$ , EtOAc/hexanes 1:1,  $R_f = 0.52$ . Mp 117–119°C. IR (neat) 3451, 3010, 1732  $cm^{-1}$ .  $^1H$  NMR (DMSO, 300 MHz)  $\delta$  7.30 (d, 2H,  $J = 8.1$  Hz), 7.22 (d, 2H,  $J = 8.1$  Hz), 5.58 (bs, 1H), 4.22 (m, 1H), 3.61 (s, 3H), 2.95 (dd, 1H,  $J = 13.8, 4.2$  Hz), 2.82 (dd, 1H,  $J = 13.8, 6.6$  Hz). MS (m/e) 216 ( $M^{2+}$ ), 214 ( $M^+$ ), 196, 125 (base peak). Anal. calcd for  $C_{10}H_{11}O_3Cl$ : C, 55.96; H, 5.16. Found: C, 55.88; H, 5.09.

## ACKNOWLEDGMENTS

The authors are grateful to Dr. Y. H. Joo, Miss S. M. Ahn, and Prof. S-K. Kang, Sung Kyun Kwan University, for valuable discussions during the preparation of this manuscript.

## REFERENCES AND NOTES

1. Sheehan, J.C.; Laubach, G.D. *J. Am. Chem. Soc.* **1951**, *73*, 4752.
2. Meyers, A.L.; Amos, R.A. *J. Am. Chem. Soc.* **1980**, *102*, 870.



3. Mori, K.; Tokigawa, T.; Matsumoto, K. *Tetrahedron* **1982**, 35, 933.
4. Brederck, H.; Gompper, R.; Theiling, G. *Ber. Deutch. Chem. Gas.* **1954**, 87, 537.
5. Thompson, J.E. *J. Org. Chem.* **1967**, 32, 3947.
6. Rubottom, G.M.; Marrero, R. *Synth. Commun.* **1981**, 11, 505.
7. Aldea, R.; Alper, H. *J. Org. Chem.* **1998**, 63, 9425.
8. Zuo, X.; Liu, H.; Liu, M. *Tetrahedron Lett.* **1998**, 39, 1941.
9. Otsubo, K.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1987**, 28, 4435.
10. Coutrot, P.; Grison, C.; Coutrot, F. *Synlett.* **1998**, 393.
11. Rho, H.S.; Ko, B.S. *Synth. Commun.* **1999**, 29, 2875.

Received in the UK September 1, 1999



## **Request Permission or Order Reprints Instantly!**

Interested in copying and sharing this article? In most cases, U.S. Copyright Law requires that you get permission from the article's rightsholder before using copyrighted content.

All information and materials found in this article, including but not limited to text, trademarks, patents, logos, graphics and images (the "Materials"), are the copyrighted works and other forms of intellectual property of Marcel Dekker, Inc., or its licensors. All rights not expressly granted are reserved.

Get permission to lawfully reproduce and distribute the Materials or order reprints quickly and painlessly. Simply click on the "Request Permission/Reprints Here" link below and follow the instructions. Visit the [U.S. Copyright Office](#) for information on Fair Use limitations of U.S. copyright law. Please refer to The Association of American Publishers' (AAP) website for guidelines on [Fair Use in the Classroom](#).

The Materials are for your personal use only and cannot be reformatted, reposted, resold or distributed by electronic means or otherwise without permission from Marcel Dekker, Inc. Marcel Dekker, Inc. grants you the limited right to display the Materials only on your personal computer or personal wireless device, and to copy and download single copies of such Materials provided that any copyright, trademark or other notice appearing on such Materials is also retained by, displayed, copied or downloaded as part of the Materials and is not removed or obscured, and provided you do not edit, modify, alter or enhance the Materials. Please refer to our [Website User Agreement](#) for more details.

**[Order now!](#)**

Reprints of this article can also be ordered at

<http://www.dekker.com/servlet/product/DOI/101081SCC100000211>