JOC*Note*

Highly Selective Methodology for the Direct Conversion of Aromatic Aldehydes to Glycol Monoesters

Hashem Sharghi* and Mona Hosseini Sarvari

Department of Chemistry, Faculty of Sciences,
Shiraz University, Shiraz 71454, I. R. Iran

shashem@chem.susc.ac.ir

Received December 2, 2002

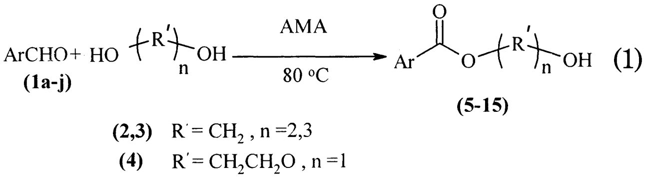
Abstract: $Al_2O_3/MeSO_3H$ (AMA) was found to be an extremely efficient reagent for the conversion of aromatic aldehydes and diols to glycol monoesters. The remarkable selectivity achieved with this reagent is an attractive feature of the present method.

Over the last 30 years, a number of methods for the conversion of aldehydes to esters have appeared in the literature.[1] The oxidation of aldehydes to carboxylic acids or esters is one of the most frequently encountered reactions in organic chemistry. Such a process has been accomplished in a variety of ways. Two-step methods include the oxidation of cyanohydrins,[2] hemiacetals,[3] acetals,[4,5] and the like. The one-pot, one-step, conventional methods reported require the use of heavy-metal oxidants such as $KMnO_4$,[6] CrO_3,[7] or the highly expensive silver,[8] ruthenium,[9] or rhodium[10] catalysts. Oxidation using alkaline iodine[11] and peroxides with chlorites[12] are the most commonly used. NIS-mediated[13] electrochemical[13] as well as very recently using H_2O_2[15] mediated oxidation of aldehydes to esters also have been reported.

Most of the reported methods were useful for oxidation of aldehydes into the corresponding esters. To our knowledge, no report has already been made on the conversion of aldehydes into glycol monoesters in the presence of diols. The synthesis of glycol monoesters of diols has received considerable interest in view of widespread applications as intermediates for sex pheromones of lepidoptera[16,17] and cross-linking agents for polyesters or fungicides.[18] The major drawbacks in the preparation of these compounds from diols include concurrent formation of diesters, necessitating a tedious separation procedure of monoesters from diprotected and unprotected diols.[19]

We have considered the usefulness of developing a convenient, efficient, and selective synthesis of glycol monoesters from the corresponding aldehydes and diols. We now report that the 1:5 molar mixture of Al_2O_3 and $MeSO_3H$ (AMA), which we have shown earlier to be an effective reagent for Fries rearrangement[20] as well as Beckmann rearrangement,[2122] is also a superior reagent for the direct conversion of aromatic aldehydes to the corresponding glycol monoesters.

Interestingly, the experimental procedure for monoesterification of aromatic aldehydes is remarkably simple and does not require the use of any solvent or inert atmosphere. Aromatic aldehydes were added to a stirred mixture of Al_2O_3 and $MeSO_3H$ (AMA), and to this was added the required diol, and the mixture was stirred at 80 °C in an oil bath (eq 1).



To establish the generality and applicability of this method, various aromatic aldehydes were subjected to the same reaction conditions to furnish the corresponding monoesters in good yields. A notable point of this method is that high yields of glycol monoesters are obtained independent of the nature of the substrate. Thus, aromatic aldehydes with electron-donating as well as electron-withdrawing substituents are both smoothly and efficiently converted to the corresponding glycol monoesters (Table 1). According to Table 1, aldehyde **1e**, which contains two hydroxy groups, underwent selective monobenzoylation of ethylene glycol to give the hydroxy monoester **9** (85%) (entry 5). In addition, 2-pyridinecarboxaldehyde **(1h)** and 1-naphthaldehyde **(1i)** were converted to the corresponding monoesters in good yields (entries 8 and 9). However, the reaction with mesitylaldehyde **(1j)** did not afforded the corresponding glycol monoester (entry 10).

Our method is applicable to other diols such as 1,3-propanediol **(3)** and diethylene glycol **(4)**. For example,

---

[*] To whom correspondence should be addressed. Tel: +98-711-2284822. Fax: +98-711-2280926.

(1) For a list of methods, see; Larock, R. C. In *Comprehensive Organic Trasformations: a Guide to Functional Group Preparations;* VHC Publications: New York, 1989; pp 840−841 and references therin.

(2) Corey, E. J.; Gilman, N. W.; Ganem, B. E. *J. Am. Chem. Soc.* **1968**, *90*, 5616.

(3) Craig, J. C.; Horning, E. C. *J. Org. Chem.* **1960**, *25*, 2098.

(4) Mavel, E. N.; Jonchich, M. J. *J. Am. Chem. Soc.* **1951**, *73*, 973.

(5) Elad, D.; Youssefyeh, R. D. *Tetrahedron Lett.* **1963**, 2189.

(6) Abiko, A.; Roberts, J. C.; Takemasa, T.; Masamune, S. *Tetrahedron Lett.* **1986**, *27*, 4537.

(7) O'Connor, B.; Just, G. *Tetrahedron Lett.* **1987**, *28*, 3235.

(8) Thomason, S. C.; Kubler, D. G. *J. Chem. Educ.* **1968**, *45*, 546.

(9) Raiendram, S.; Trivedi, D. C. *Synthesis* **1995**, 153.

(10) Grigg, R.; Mitchell, T. R. B.; Sutthivaiyakit, S. *Tetrahedron* **1981**, *37*, 4313.

(11) Yamada, S.; Morizono, D.; Yamamoto, K. *Tetrahedron Lett.* **1992**, *33*, 4329.

(12) Dalcanal, E.; Montanari, F. *J. Org. Chem.* **1986**, *51*, 567.

(13) McDonald, C.; Holcomb, H.; Kennedy, K.; Kirkpatrick, E.; Leathers, T.; Vanemon, P. *J. Org. Chem.* **1989**, *45*, 1213.

(14) Okimoto, M.; Chiba, T. *J. Org. Chem.* **1988**, *53*, 218.

(15) Gopinath, R.; Patel, B. K. *Org. Lett.* **2000**, *2*, 577. Sato, K.; Hyodo, M.; Takagi, J.; Aoki, M.; Noyori, R. *Tetrahedron Lett.* **2000**, *41*, 1439.

(16) Leznoff, C. C. *Acc. Chem. Res.* **1978**, *11*, 327.

(17) (a) Henrick, C. A. *Tetrahedron* **1977**, *33*, 1845. (b) Rossi, R. *Synthesis* **1971**, 817.

(18) Hosokawa, T.; Imada, Y.; Murahashi, S. I. *J. Chem. Soc., Chem. Commun.* **1983**, 1245.

(19) Babler, J. H.; Coghlan, M. J. *Tetrahedron Lett.* **1979**, *20*, 1971.

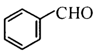
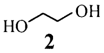
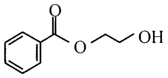
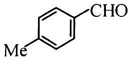
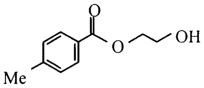
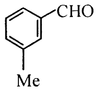
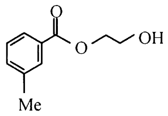
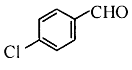
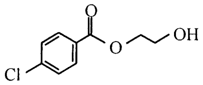
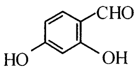
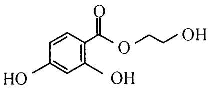
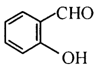
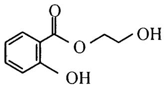
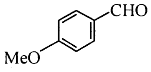
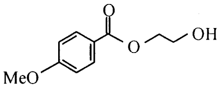
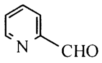
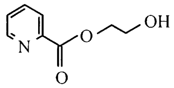
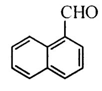
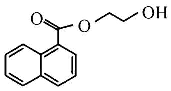
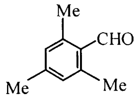
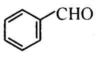
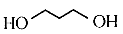
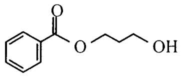
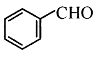
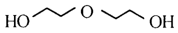
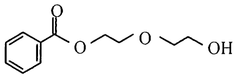
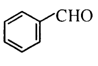
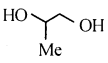
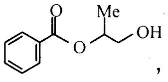
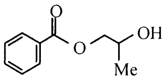
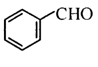
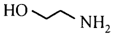
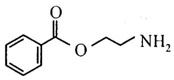
(20) Sharghi, H.; Kaboudin, B. *J. Chem. Res., Synop.* **1998**, 629.

(21) Sharghi, H.; Hosseini Sarvari, M. *J. Chem. Res., Synop.* **2001**, 446.

(22) Choudary, B. M.; Reddy, P. N. *Synlett* **1995**, 959.

10.1021/jo020724o CCC: $25.00

TABLE 1. Conversion of Aldehydes into Glycol Monoesters Using AMA

Entry	Aldehydes **(1a-j)**	Time/h.	Diols **(2-6)**	Products **(5-18)**	Yields[a] %
1	 **1a**	4	 **2**	 **5**[b]	80
2	 **1b**	3	**2**	 **6**[b]	85
3	 **1c**	2	**2**	 **7**	70
4	 **1d**	4	**2**	 **8**[b]	80
5	 **1e**	2.5	**2**	 **9**	85
6	 **1f**	3	**2**	 **10**	84
7	 **1g**	5.5	**2**	 **11**	76
8	 **1h**	3	**2**	 **12**	82
9	 **1i**	5.5	**2**	 **13**	76
10	 **1j**	10	**2**	**No reaction**	-----
11	 **1a**	4.5	 **3**	 **14**[b]	74
12	 **1a**	6	 **4**	 **15**	76
13	 **1a**	4.5	 **5**	 **16** [b] ,  **17** [b]	95 (1:1)[c]
14	 **1a**	4.5	 **6**	 **18**	81

[a] Isolated yields. [b] These compounds are known, and only ^{1}H NMR and/or IR spectra data are presented here. [c] The ratio of the products were estimated by^{1}H NMR integration.

1,3-propanediol **(3)** was also monobenzoylated with a high selectivity, but the yield was less than those involving ethylene glycol (entries 1 and 11). Benzaldehyde can also be converted to the corresponding glycol monoester **15** when treated with diethylene glycol **(4)**. This reaction constitutes the first satisfactory method for the direct synthesis of diethylene glycol monobenzoate **15** (entry 12). Glycol monoesters such as those of ethylene glycol have been used as cross-linking agents for polyesters or as fungicides. The present method indirectly provides a useful means for the selective monoprotection of some diols. We believe that this constitutes the first satisfactory method for the direct conversion of aldehydes to the corresponding glycol monoesters. Exhaustive CAS searches have led us to this conclusion.

This method is useful for the selective monoprotection of unsymmetrical glycols when in fact a mixture of presumably difficulty separable products is obtained (entry 13). Finally, it is interesting to note that the amino alcohols such as 2-amino-1-ethanol **(6)** selectively gave the corresponding amino ester **(18)** (81%) (entry 14).

No attempt has been made to probe the mechanism of the reaction. Mechanistically, it seems plausible that the Bayer−Villiger oxidation reaction occurs first and the esterification step follows next. However, the reaction failed in the absence of oxygen attempted under nitrogen atmosphere. Thus, the aldehyde is oxidized by air in the presence of AMA to the corresponding carboxylic acid, which is then esterified selectively with diol. The selectivity behavior of this reaction has become not clear to us yet, and no evidence is merging for a convincing explanation. In fact, the reaction dose not occur without alumina and/or sulfonic acid.

In conclusion, the presented method constitutes the first satisfactory method for the direct conversion of aldehydes to glycol monoesters. Solvent-free conditions, high yields, use of commercially available reagents, simple workup, and high selectivity can make this procedure a useful and attractive method for the synthesis of glycol monoesters.

Experimental Section

General Procedure. To a mixture of $MeSO_3H$ 98% (1 mL, 15 mmol) and Al_2O_3 (acidic type 540 C, 0.27 g, 3 mmol) were added the appropriate aldehyde (1 mmol) and then diol (1 mmol). The mixture was stirred and heated in an oil bath at 80 °C for 2−10 h (see Table 1). The mixture was then poured into water and extracted two times with ethyl acetate (20 mL). The organic layer was washed with a saturated solution of sodium bicarbonate (30 mL). The organic layer was dried ($CaCl_2$) and evaporated in vacuo to give a residue that was almost a pure glycol monoester product. Further purification of the products was carried out by silica gel short column chromatography.

2-Hydroxyethyl benzoate (5):[22] ^{1}H NMR ($CDCl_3$, 250 MHz) δ 3.96 (t, 2H), 4.45 (t, 2H), 7.49−7.58 (m, 3H), 8.1 (d, 2H); IR (neat) 1718 cm^{-1}.

2-Hydroxyethyl 4-methylbenzoate (6):[22] ^{1}H NMR ($CDCl_3$, 250 MHz) δ 2.39 (s, 3H), 3.88 (t, 2H), 4.41 (t, 2H), 7.2−7.31 (m, 2H), 7.91 (m, 2H); IR (neat) 1720 cm^{-1}.

2-Hydroxyethyl 4-chlorobenzoate (8):[22] ^{1}H NMR ($CDCl_3$, 250 MHz) δ 3.98 (t, 2H), 4.45 (t, 2H), 7.43 (d, 2H), 7.14 (d, 2H); IR (neat) 1712 cm^{-1}.

2-Hydroxypropyl benzoate (14):[22] ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.99 (m, 2H), 3.78 (t, 2H), 4.45 (t, 2H), 7.41−7.58 (m, 3H), 8.05 (d, 2H); IR (neat) 1718 cm^{-1}.

2-Hydroxy-1-methylethyl benzoate (16):[22] ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.27 (m, 3H), 3.76 (d, 2H), 5.21 (m, 1H), 7.42−7.56 (m, 3H), 8.04 (d, 2H); IR (neat) 1722 cm^{-1}.

2-Hydroxy-2-methylethyl benzoate (17):[22] ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.35 (m, 3H), 4.16−4.31 (t, 3H), 7.42−7.56 (m, 3H), 8.04 (d, 2H); IR (neat) 1722 cm^{-1}.

2-Hydroxyethyl 3-methylbenzoate (7): ^{1}H NMR ($CDCl_3$, 250 MHz) δ 2.37 (s, 3H), 3.94 (t, 2H), 4.43 (t, 2H), 7.19−7.37 (m, 2H), 7.83−8.18 (m, 2H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 21.49, 61.16, 67.79, 127.14, 128.59, 130.16, 130.49, 134.20, 138.46, 167.46; IR (neat) 3440, 1715, 1610, 1580, 1450, 1370, 1280, 1200, 1115, 1080, 925, 740, 680 cm^{-1}; MS (*m/e*) 180 (3.5, M^{+}), 163 (51.6), 119 (base peak), 91 (31.7). Anal. Calcd for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.52; H, 6.50.

2-Hydroxyethyl 2,4-dihydroxybenzoate (9): ^{1}H NMR (DMSO d_6, 250 MHz) δ 3.7 (t, 2H), 4.28 (t, 2H), 6.3 (s, 1H), 6.38 (d, 1H) 7.72 (d, 1H); ^{13}C NMR (DMSO-d_6, 62.9 MHz) δ 59.28, 66.79, 102.75, 104.37, 108.59, 132.18, 163.10, 164.56, 169.62; IR (neat) 3312, 1700, 1625, 1515, 1425, 1390, 1315, 1266, 1210, 1150, 1100, 1066, 999, 900, 834 cm^{-1}; MS (*m/e*) 198 (28.6, M^{+}), 180 (32.9), 137 (74), 136 (base peak), 108 (43.9). Anal. Calcd for $C_9H_{10}O_5$: C, 54.55; H, 5.09. Found: C, 54.31; H, 4.97.

2-Hydroxyethyl 2-hydroxybenzoate (10): ^{1}H NMR (DMSO-d_6, 250 MHz) δ 3.94 (t, 2H), 4.45 (t, 2H), 6.86 (m, 1H), 6.96 (m, 2H), 7.46 (m, 1H) 7.86 (m,1H); ^{13}C NMR (DMSO-d_6, 62.9 MHz) δ 61.37, 63.92, 118.04, 119.68, 130.35, 136.21, 162.09, 170.22; IR (neat) 3340, 1720, 1625, 1517, 1430, 1390, 1324, 1268, 1206, 1153, 1100, 1066, 997, 897, 834 cm^{-1}; MS (*m/e*) 182 (20, M^{+}), 160 (35), 121 (65), 120 (base peak), 93 (41). Anal. Calcd for $C_9H_{10}O_4$: C, 59.34; H, 5.53. Found: C, 59.23; H, 5.26.

2-Hydroxyethyl 4-methoxybenzoate (11): ^{1}H NMR ($CDCl_3$, 250 MHz) δ 3.82 (s, 3H), 3.88 (t, 2H), 4.20 (t, 2H), 6.99 (d, 2H), 7.92 (d, 2H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 55.25, 61.71, 65.90, 113.3, 120.82, 131.50, 162.48, 165.66; IR (neat) 3440, 1720, 1600, 1590, 1455, 1430, 1280, 1230, 1180, 1110, 1080, 1045, 755, 665 cm^{-1}; MS (*m/e*) 196 (34, M^{+}), 151 (62), 135 (43.2), 107 (base peak). Anal. Calcd for $C_{10}H_{12}O_4$: C, 61.22; H, 6.16. Found: C, 61.07; H, 5.98.

2-Hydroxyethyl nicotinate (12): ^{1}H NMR (CCl_4, TMS, 250 MHz) δ 3.95 (t, 2H), 4.47 (t, 2H), 7.46 (m, 1H), 7.82 (m, 1H), 8.11 (m, 1H), 8.69 (m, 1H); ^{13}C NMR (CCl_4, TMS, 62.9 MHz) δ 61.69, 66.32, 122.61, 128.10, 136.01, 147.3, 147.6, 165.01; IR (neat) 3400, 1725, 1590, 1495, 1452, 1310, 1293, 1250, 1124, 1075, 800, 750, 701, 665 cm^{-1}; MS (*m/e*) 167 (19.9, M^{+}), 150 (12.4), 124 (13.5), 106 (40.7), 78 (base peak), 51 (65.6). Anal. Calcd for $C_8H_9NO_3$: C, 57.48; H, 5.43. Found: C, 57.11; H, 5.24.

2-Hydroxyethyl 1-naphthoate (13): ^{1}H NMR ($CDCl_3$, 250 MHz) δ 3.81 (t, 2H), 4.35 (t, 2H), 7.28−7.48 (m, 3H), 7.7 (d, 1H), 7.82 (d, 1H), 8.04 (d, 1H), 8.75(d, 1H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 61.40, 66.86, 124.87−134.18, 168.08; IR (neat) 3500, 1715, 1600, 1520, 1360, 1285, 1250, 1205, 1180, 1140, 1050, 960, 790 cm^{-1}; MS (*m/e*) 216 (25.1, M^{+}), 199 (18.2), 172 (30.2), 155 (base peak), 127 (48.9). Anal. Calcd for $C_{13}H_{12}O_3$: C, 72.21; H, 5.59. Found: C, 71.98; H, 5.31.

Diethylene glycol monobenzoate (15): ^{1}H NMR ($CDCl_3$, 250 MHz) δ 3.72 (m, 4H), 3.85 (t, 2H), 4.50 (t, 2H), 7.41−7.59 (m, 3H), 8.06 (d, 2H); ^{13}C NMR ($CDCl_3$) δ 63.20, 64.91, 66.18, 68.65, 130.53, 131.82, 132.07, 135.29, 169.14; IR (neat) 3416, 2916, 1717, 1600, 1449, 1320, 1274, 1200, 1165, 1130, 1066, 1033, 890 cm^{-1}; MS (*m/e*) 210 (1.1, M^{+}), 149 (19.7), 105 (100), 77 (31.6), 45 (32.5). Anal. Calcd for $C_{11}H_{14}O_4$: C, 62.85; H, 6.71. Found: C, 62.69; H, 6.58.

2-Aminoethyl Benzoate (18). To a mixture of $MeSO_3H$ 98% (1 mL, 15 mmol) and Al_2O_3 (acidic type 540 C, 0.27 g, 3 mmol) were added benzaldehyde (1 mmol) and then 2-amino-1-ethanol (1 mmol). The mixture was stirred and heated in an oil bath at 80 °C for 4.5 h (Table 1, entry 14). The mixture was poured into a saturated solution of sodium bicarbonate and extracted two times with ethyl acetate (20 mL). Then organic layer was dried ($CaCl_2$) and evaporated in vacuo to give 2-aminoethyl benzoate **(18)** (81%): ^{1}H NMR ($CDCl_3$, 250 MHz) δ 3.53 (t, 2H), 3.73 (t, 2H), 4.67 (s, 2H), 7.31 (m, 3H), 7.74 (d, 2H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 43.19, 61.98, 127.44, 128.87, 130.09, 133.69, 169.19; IR (neat) 3357, 3074, 2948, 1724, 1652, 1556, 1519, 1388, 1313, 1974, 806, 717 cm^{-1}; MS (*m/e*) 165 (10.3, M$^+$), 149 (48.9), 105 (100), 77 (31.6). Anal. Calcd for $C_9H_{11}NO_2$: C, 65.44; H, 6.71. Found: C, 65.27; H, 6.52.

Acknowledgment. We gratefully acknowledge the support of this work by the Shiraz University Research Council and Associated Professor M. H. Ghatee for his helpful comments.

Supporting Information Available: Copies of ^{1}H NMR and IR of compounds **5**, **6**, **8**, **14**, **16**, and **17** and spectra data of compounds **7**, **9**−**13**, **15**, **18**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO020724O