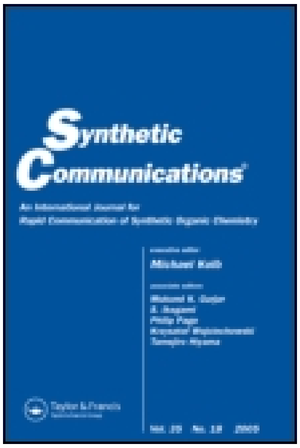
This article was downloaded by: [Fordham University]
On: 29 October 2013, At: 22:25
Publisher: Taylor & Francis
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



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/lsyc20

Practical Preparation of Esters and Thioacetates from Alkyl Halides and Carboxylates or Thioacetate Catalyzed by PEG400 without Solvent

Yu-Qing Cao [a] , Guo-Qiang Wu [a] , Ya-Bin Li [a] , Zhi Dai [a] & Bao-Hua Chen [a]
[a] College of Pharmacy, Hebei University , Baoding, China

Published online: 23 Nov 2006.

To cite this article: Yu-Qing Cao , Guo-Qiang Wu , Ya-Bin Li , Zhi Dai & Bao-Hua Chen (2006) Practical Preparation of Esters and Thioacetates from Alkyl Halides and Carboxylates or Thioacetate Catalyzed by PEG400 without Solvent, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 36:22, 3353-3358, DOI: 10.1080/00397910600941380

To link to this article: http://dx.doi.org/10.1080/00397910600941380

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®, 36: 3353–3358, 2006
Copyright © Taylor & Francis Group, LLC
ISSN 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910600941380

Practical Preparation of Esters and Thioacetates from Alkyl Halides and Carboxylates or Thioacetate Catalyzed by PEG400 without Solvent

Yu-Qing Cao, Guo-Qiang Wu, Ya-Bin Li, Zhi Dai, and Bao-Hua Chen
College of Pharmacy, Hebei University, Baoding, China

Abstract: Carboxylic esters and thioacetates were conveniently prepared in good to excellent yields under mild conditions by the reaction of alkyl halides with sodium carboxylates or sodium thioacetate catalyzed by PEG400 in the absence of solvents.

Keywords: Alkyl halides, carboxylic esters, PEG400, solventless, thioacetates

INTRODUCTION

Carboxylic esters and thioesters were widely used as intermediates in organic synthesis and as products in pharmaceutical and spice industries[1] and had attracted a great deal of attention. For example, they can be applied in the synthesis of α,β-unsaturated esters and lactones under very mild conditions.[2] One of traditional methods for the preparation of carboxylic esters was the reaction of an alcohol with a carboxylic acid, which usually was catalyzed by acids. Long reaction times were needed.[3] Another way to make esters was to turn the acid into acyl chloride and then added the alcohol along with base.[4] On the other hand, the most traditional methods for the preparation of thiolesters were the coupling of a thiol with a carboxylic acid[5] or an alcohol with a thiocarboxylic acid.[6] However, the former strategy

Received in R.O.C. January 16, 2006

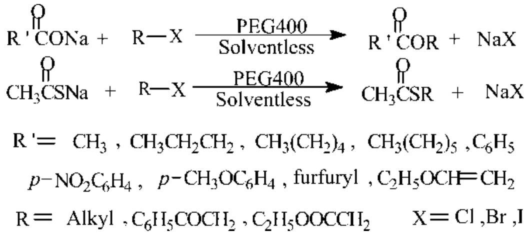
Address correspondence to Yu-Qing Cao, College of Pharmacy, Hebei University, Baoding 071002, China. E-mail: pharm_hbu@yahoo.com

needs long reaction times and the latter needs the participation of precious dehydrating agents such as dicyclohexylcarbodimide (DCC), because of its small equilibrium constants.

The reaction of alkyl halides with sodium carboxylates or sodium thioacetate was a common method for the preparation of carboxylic esters or thioacetates.[7,8] The advantages of this reaction were shorter reaction times, mild conditions, and higher yields. This method was especially applicable for the preparation of carboxylic esters or thioacetates that had unsaturated bonds, but the most of reactions were carried out in organic solvents. Developing green chemistry is one of the most important purposes of organic synthesis at present. Organic synthesis in the absence of solvent was of great value.[9,10] In this respect, a method that involves the application of readily available reagents, such as alkyl halides and sodium carboxylates or sodium thioacetates in solvent-free conditions, should be interesting and easily put into industrial production.

Polyethylene glycols (PEGs) could be regarded as the acyclic crown ether and had been widely used as phase-transfer catalysts (PTC) in many organic reactions owing to their stability, low cost, low toxicity, and easy availability.[11,12] PEG with 7–9 units was more effective in catalyzing the reactions in which Na^+ salts participated. Especially because of the liquid property, perfect solubility in water, and the participation of two hydroxy groups during the destructing crystal lattice of the solids, PEG400 was more suitable for solid–liquid-phase solvent-free organic reactions. The carboxylate anions or thioacetic anions could easily enter the liquid phase and become strong nucleophilic reagents that could promptly undertake nucleophilic substitution.

In continuation of our research on the use of PEGs as PTCs in organic synthesis without solvents,[13–15] we herein report a facile method for the preparation of carboxylic esters or thioacetates by the reaction of alkyl halides with sodium carboxylates or sodium thioacetate, catalyzed by PEG400 in the absence of solvents (Scheme 1). The experimental results are listed in Table 1.



Scheme 1.

Table 1. Esterification of sodium carboxylate with alkyl halides

Entry	R′	Alkyl halides	Time (h)	Yield (%)	Bp (°C/mmHg) or mp (°C)	
					Found	Reported
1	CH_3-	n-butyl-Cl	5	89	124–125/760	124–126/760[16]
2	CH_3-	n-butyl-Br	4	90		
3	CH_3-	n-butyl-I	2	90		
4	CH_3-	n-$C_6H_{13}Br$	4	92	171–172/760	171–173/760[17]
5	CH_3-	n-$C_8H_{17}Br$	5	91	121–122/50	210–212/760[16]
6	CH_3-	s-butyl-Br	5	68	39–40/50	111–112/760[16]
7	CH_3-	t-butyl-Br	7	41	30–31/50	98–99/760[16]
8	CH_3-	c-C_6H_{11}-Br	6	85	87–88/50	172–173/760[16]
9	CH_3-	$C_6H_5CH_2Cl$	4.5	94	115–116/50	206–208/760[16]
10	CH_3-	$CH_2{=}CHCH_2Br$	3	86	103–104/760	103–105/760[17]
11	CH_3-	$C_6H_5COCH_2Br$	2	77	49–50	49–51[16]
12	CH_3-	$C_2H_5OOCCH_2Br$	2.5	81	178–179/760	179–180/760[17]
13	$CH_3CH_2CH_2$-	n-butyl-Br	3.5	90	163–164/760	164–165/760[16]
14	$CH_3CH_2CH_2$-	$C_6H_5CH_2Cl$	4	95	144–145/50	240–241/760[16]
15	$CH_3(CH_2)_4$-	$CH_2{=}CHCH_2Br$	4	88	183–184/760	184–186/760[16]
16	$CH_3(CH_2)_5$-	$CH_2{=}CHCH_2Br$	5	89	209–210/760	210–211/760[16]
17	Ph-	n-butyl-Br	5	87	166–167/50	248–250/760[16]
18	Ph-	n-$C_6H_{13}Br$	6	88	182–183/50	272–273/760[16]
19	Ph-	$C_6H_5CH_2Cl$	6.5	90	18–20	19–20[16]
20	Ph-	$CH_2{=}CHCH_2Br$	4	86	162–163/50	243–244/760[17]
21	p-$NO_2C_6H_4$-	n-butyl-Br	10	76	36–37	37–38[17]
22	p-$CH_3OC_6H_4$-	n-butyl-Br	4	90	183–184/40	184–185/40[17]
23	furfuryl	C_2H_5Br	5	82	110–111/50	196–197/760[17]
24	$C_2H_5OCH{=}CH$-	C_2H_5Br	4	81	109–110/50	195–195/760[17]

RESULTS AND DISCUSSION

Taking the reaction of sodium acetate and benzyl chloride as an example, we found that a yield as low as 67% was obtained after the reaction was performed over 12 h without the presence of PEG400. However, when 3 mol% of PEG400 was added, the reaction period was greatly shortened, and the yield was 94%. This amount, 3% mol of PEG400, was adequate to catalyze the reaction effectively. The more PEG400 was employed, the more products were lost during washing with water.

To shorten the reaction time, the reactions of sodium carboxylates and alkyl halides were heated at 65–70°C. As shown as in Table 1, the yield of n-butyl acetate was slightly lower than benzyl acetate because some of esters with low molecular weight were lost in the washing process. Longer reaction periods were needed for the reactions of sodium benzoate than sodium acetate. The esterification of sodium benzoate with electron-donating groups such as -OCH_3 in the aromatic ring and alkyl halides could be carried out in relatively shorter time than with electron-withdrawing groups such as -NO_2. Especially for entries 11 and 12, the yields were relatively lower, because some condensation products were obtained as the high activity of the α-position of carbonyl group.

It can be inferred that alkyl iodide was more active than alkyl bromide, which was also more active than alkyl chloride. We can consider the mechanism as SN_2 substitution reactions. Longer reaction time was needed for cyclohexyl bromide because of the steric effect of the cyclohexyl ring. The reaction of sodium acetate and s-butyl bromide could be carried out in lower yields than n-butyl bromide, whereas very low yields were obtained in the reactions of sodium acetate and t-butyl bromide. We proposed that the side reaction of the competitive elimination for the t-butyl bromide and s-butyl bromide might be the main reason for the low yields.

Table 2. Esterification of sodium thioacetate with alkyl halides

Entry	Alkyl halides	Time (h)	Yield (%)	Bp (°C/mmHg) or mp (°)	
				Found	Reported
1	n-butyl-Cl	4	91	162–164/760	163–164/760[18]
2	n-butyl-Br	3	93		
3	n-butyl-I	1.5	93		
4	c-C_6H_{11}-Br	5	79	116–118/50	90–91/15[18]
5	n-C_8H_{17}-Br	4	95	146–148/50	128–131/24[18]
6	t-butyl-Br	7	62	56–57/50	130/760[18]
7	$C_6H_5CH_2$-Cl	3	93	160–162/50	247–250/760[18]
8	CH_2=CH-CH_2-Br	2	91	125–127/760	126–128/760[18]
9	$C_6H_5COCH_2$-Br	1.5	85	130–132/50	108–110/18[18]
10	$C_2H_5OOCCH_2$-Br	1.5	89	82–83/50	64–65/18[18]

Based on the results listed in Table 2, the substitution of some alkyl halides with sodium thioacetates could be carried out at room temperature, and relatively higher yields could be obtained than with sodium acetates, especially for entry 6 in Table 2. The reason was that thioacetic ion had stronger nucleophilicity and weaker basicity than the carboxylic ion.

In conclusion, we have demonstrated a convenient and efficient method for preparing esters or thioacetates from the corresponding alkyl halides and sodium carboxylates or sodium thioacetate catalyzed by PEG400 without solvent. The advantages of this procedure are higher yield, operational simplicity, low cost, and less pollution to environment. We assume that the method is suitable for industrial application.

EXPERIMENTAL

GC-17A is a column packed with SE30 on Chromsorb using o-terphenyl as an internal standard. Thin-layer chromatography was GF254 TLC with petroleum ether/ethyl acetate (10/1) as eluent. Alkyl halides, sodium carboxylate, sodium thioacetate, and PEG400 were commercially available and used without further purification. Melting points were determined on a microscopy apparatus and are uncorrected

Typical Procedure for the Preparation of Benzyl Acetate

A mixture of sodium acetate (18 g, 0.22 mol), benzyl chloride (25.4 g, 0.2 mol), and PEG400 (2.4 g, 0.006 mol) was stirred in a 50 mL, three-necked, round-bottomed flask equipped with a mechanical stirrer. Then the mixture was vigorously stirred at 65–70°C. The progress of the reaction was monitored by TLC. Upon completion, the reaction mixture was washed with 50 ml of water three times. The organic phase was separated and dried over magnesium sulfate. Then 28.2 g of benzyl acetate were collected at 115–116°C/50 mmHg. Identification was based on comparison with physical data reported in the literature.

Typical Procedure for the Preparation of Benzyl Thioacetate

A mixture of sodium thioacetate (21.6 g, 0.22 mol), benzyl chloride (25.4 g, 0.2 mol), and PEG400 (2.4 g, 0.006 mol) was stirred in a 50 mL, three-necked, round-bottomed flask equipped with a mechanical stirrer. Then the mixture was vigorously stirred at room temperature. The progress of the reaction was monitored by TLC. Upon completion, the reaction mixture was washed with 50 ml of water three times. The organic phase was separated and dried over magnesium sulfate. Then 31.9 g of benzyl thioacetate was collected at 160–162°C/50 mmHg. The product was identified by comparison with physical data reported in the literature.

REFERENCES

1. Welch, S. L.; Wong, P. Y. A synthetic precursor of (±)-trichodermin. *Tetrahedron Lett* **1972**, *19*, 1853.
2. Gurudutt, K. N.; Rao, S.; Srinivas, P.; Srinivas, S. Nucleophilic substitution of SN_1-active halides using zinc salts: Preparation of thiolacetates. *Tetrahedron* **1995**, *51*, 3045.
3. Lee, J. C.; Choi, Y. An improved method for preparation of carboxylic esters using CsF-celite/alkyl halide/CH_3CN. *Synth. Commun.* **1998**, *28*, 2021.
4. Kaiser, E. M.; Woodruff, R. A. Synthesis of esters of acid-unstable alcohols by means of n-butyllithium. *J. Org. Chem.* **1970**, *35*, 1198.
5. Imanoto, T.; Kodera, M.; Yokoyama, M. A convenient method for the preparation of thiol esters. *Synthesis* **1982**, *2*, 134.
6. Grunwell, J. R.; Foerst, D. L. The synthesis of thiol esters with dicyclohexylcarbodiimide. *Synth. Commun.* **1976**, *6*, 453.
7. Pfeffer, P. E.; Foglia, T. A.; Barr, P. A.; Schmeltz, I.; Silbert, L. S. Esterification of hindered carboxylic acids: Alkylation of carboxylate salts. *Tetrahedron Lett.* **1972**, *40*, 4063.
8. Anthony, G. M. B.; Nobuyuki, K.; Panayiotis, A. P. *Chem. Commun.* **1995**, *14*, 1403.
9. Wang, X. C.; Li, Z.; Da, Y. X.; Chen, J. C. Phase transfer catalyzed synthesis of 4-carboxyl-phenoxyacetic acid derivatives. *Synth. Commun.* **1999**, *29*, 4153.
10. Li, P.; Alper, H. Poly(ethylene glycol) promoted reactions of vinylic dibromides: Dehydrohalogenation and palladium(0)-catalyzed formal oxidative homologation. *J. Org. Chem.* **1986**, *51*, 4354.
11. Tannaka, K.; Toda, F. Solvent-free organic synthesis. *Chem. Rev.* **2000**, *100*, 1025.
12. Lonpy, A.; Song, S. J.; Sohn, S. M.; Lee, Y. M.; Kwon, T. W. Solvent-free bentonite-catalyzed condensation of malonic acid and aromatic aldehydes under microwave irradiation. *J. Chem. Soc., Perkin Trans 1* **2001**, 1220.
13. Cao, Y. Q.; Chen, B. H.; Pei, B. G. Cyanidation of halogen compounds and esters catalyzed by PEG400 without solvent. *Synth. Commun.* **2001**, *31*, 2202.
14. Du, Y. F.; Cao, Y. Q.; Dai, Z.; Chen, B. H. A study on the heterogeneous reaction of trialkylsilyl chlorides with inorganic salts and monocarboxylates catalyzed by PEG400. *J. Chem. Res., Synop.* **2004**, 223.
15. Cao, Y. Q.; Dai, Z.; Zhang, R.; Chen, B. H. A practical Knoevenagel condensation catalyzed by PEG400 and anhydrous K_2CO_3 without solvent. *Synth. Commun.* **2004**, *34*, 2965.
16. Windholz, M. *The Merck Index*, 10th ed.; Merck & Co., Inc., 1983.
17. Cagogan, J. I.; Pattenden, G.; Rees, C. W. *Dictionary of Organic Compounds, 6th ed.*; Chapman and Hall: London, 1996.
18. Cainelli, G.; Contento, M.; Manscalchi, F.; Mussatto, M. C. The use of polymer supported thioacetate ion as a convenient way to introduce sulfur into organic molecules. *Synthesis* **1981**, *4*, 302.