Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron Letters 49 (2008) 1115–1120
Tetrahedron Letters

A simple procedure for the esterification of alcohols with sodium carboxylate salts using 1-tosylimidazole (TsIm)

Mohammad Navid Soltani Rad [a,*], Somayeh Behrouz [b], Mohammad Ali Faghihi [b], Ali Khalafi-Nezhad [a]

[a] Department of Chemistry, Faculty of Basic Sciences, Shiraz University of Technology, Shiraz 71555-313, Iran
[b] Department of Chemistry, College of Sciences, Shiraz University, Shiraz 71454, Iran

Received 7 November 2007; revised 5 December 2007; accepted 12 December 2007

Abstract

An efficient and selective method for esterification of alcohols using *N*-(*p*-toluenesulfonyl)imidazole (TsIm) is described. In this method, alcohols are refluxed with a mixture of RCO_2Na (R: alkyl and aryl), TsIm, and triethylamine in the presence of catalytic amounts of tetra-*n*-butylammonium iodide (TBAI) in DMF to afford the corresponding esters in good yields. This methodology is highly efficient for various structurally diverse alcohols with selectivity for ROH: $1^\circ > 2^\circ > 3^\circ$.

Keywords: Esterification; Alcohol; Carboxylic salts; Triethylamine (TEA); *N*-(*p*-Toluenesulfonyl)imidazole (TsIm); Tetrabutylammonium iodide (TBAI)

Esterification is an important reaction due to the wide utility of esters in organic and bioorganic synthesis.[1] Esterification is extensively employed for the protection and further manipulation of the carboxylic acid functional group as well as the synthesis of natural products. There are numerous general methods for accessing carboxylic esters.[1,2] Among these, the direct esterification reaction of carboxylic acids with alcohols in the presence of a large number of different reagents and various conditions was established.[1,2] Moreover, the esterification of carboxylic acids or their salts with carbon electrophiles such as alkyl halides,[3] sulfonates,[3b,4] epoxides,[5] aziridines,[6] diazo compounds,[7] quaternary ammonium salts,[8] oxonium ions,[9] acetals,[10] trialkyl phosphates,[11] trialkyl phosphites,[12] methyltrialkoxy phosphonium tetrafluoborate salts,[13] *t*-butyl ethers,[14] ditosylamines,[15] strained cycloalkanes,[16] and multiple bonds[17] is a well-known procedure. The reaction of carboxylic salts with carbon electrophiles is usually preferred because of easier handling, higher nucleophilicity, simpler work-up, and cleaner reaction in comparison with carboxylic acids. In view of the wide diversity of alcohols with respect to alkyl halides, the reaction of carboxylic salts with alcohols would seem to be a suitable and attractive strategy, and indeed there are a few reports that have exemplified the esterification of alcohols via carboxylic salts including Mitsunobu conditions[18] using sodium[19] or zinc[20] carboxylate/Ph_3P/diethyl azodicarboxylate (DEAD) or diisopropyl azodicarboxylate (DIAD) and potassium carboxylate/Ph_3P/CCl_4.[21] The aforementioned methods have several drawbacks such as non-generality for various types of alcohols and carboxylic acids, the use of expensive DEAD or DIAD, low yields, long reaction times, tedious work-up as well as cumbersome separation from the generated $Ph_3P{=}O$, and unreacted Ph_3P. Hence, there is still a need to develop practical and convenient methods for the esterification of alcohols with carboxylate salts. Recently, we reported 1-tosylimidazole (TsIm) as a highly efficient, cheap and stable reagent for the one-pot conversion of alcohols to alkyl azides[22a] and nitriles.[22b] In continuation of our interest in the application of TsIm in organic

* Corresponding author. Tel.: +98 711 7261392; fax: +98 711 7354523.
E-mail addresses: soltani@sutech.ac.ir, nsoltanirad@gmail.com (M. N. Soltani Rad).

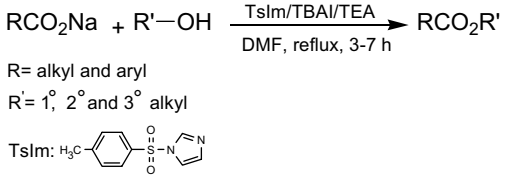
0040-4039/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2007.12.068

synthesis, herein, we report that 1°, 2°, and 3° alcohols can be converted efficiently into their corresponding esters using TsIm/RCO_2Na in the presence of triethylamine (TEA) and catalytic amounts of TBAI in DMF (Scheme 1).

The first step of this synthetic approach involved optimization of the reaction conditions. Initially, the effect of various solvents on the model reaction of 2-phenylethanol, excess sodium benzoate (2.0 equiv) and freshly prepared TsIm[22a] (1.2 equiv) in the presence of a catalytic amount of TBAI was studied. The results are depicted in Table 1.

As the data in Table 1 indicates, DMF (entry 2) was the most efficient solvent. Using anhydrous DMF, DMSO, and HMPA (Table 1, entries 1, 3, and 6) afforded moderate yields of the corresponding ester. The choice of the base for activation of the alcohols for reaction with TsIm had a great significance. In this case, we evaluated the potency of several organic and inorganic bases on the model reaction (Table 2). As the results in Table 2 indicate, TEA (Table 2, entry 7) proved to be the most efficient base for activation of 2-phenylethanol. Other bases afforded lower yields of phenethyl benzoate.

We also studied the role of tetra-*n*-butylammonium salts as phase transfer catalysts (PTC) on the model reaction (Table 3). In the absence of PTC the reaction occurred but only in moderate yield. However, using TBAI shortened the reaction time and an improved yield was obtained. The use of an equimolar mixture of TBAI and TBAB (Table 3, entry 7) gave no improvement in reaction. Other PTCs (Table 3, entries 2–4 and 6) were not as effective as TBAI (Table 3, entry 5). To determine whether iodide in TBAI was responsible for catalysis of the reaction, we examined other iodide sources including LiI, NaI, and KI for the conversion of 2-phenylethanol into phenethyl benzoate. Lower yields of 49%, 51%, and 60% were obtained.



Scheme 1.

Table 1
Effect of various solvents on the conversion of 2-phenylethanol into phenethyl benzoate

Entry	Solvent	Time (h)	Yield[b] (%)
1	DMF[a]	6	55
2	DMF	3	94
3	DMSO	6	48
4	THF	48	NR[c]
5	MeCN	12	10
6	HMPA	6	50
7	Toluene	48	NR
8	Acetone/H_2O[d]	18	Trace
9	H_2O	48	NR

[a] Anhydrous DMF.
[b] Isolated yield.
[c] No reaction.
[d] (1:1) ratio.

Table 2
Effect of various bases on the conversion of 2-phenylethanol into phenethyl benzoate

Entry	Base	Time (h)	Yield[b] (%)
1	DBU	7	55
2	DABCO	8	40
3	DMAP	8	31
4	MgO	6	47
5	Cs_2CO_3	6	50
6	K_2CO_3	8	47
7	TEA	3	94
8	NaH	8	15
9	Al_2O_3[a]	8	20

[a] Basic alumina.
[b] Isolated yield.

Table 3
Effect of various PTCs on the conversion of 2-phenylethanol into phenethyl benzoate

Entry	PTC	Time (h)	Yield[b] (%)
1	None	7	40
2	TBAF	9	47
3	TBAC	9	52
4	TBAB	6	60
5	TBAI	3	94
6	$(n\text{-Bu})_4NHSO_4$[a]	9	43
7	TBAI/TBAB[c]	7	70

[a] Two equivalents of TEA were used.
[b] Isolated yield.
[c] (1:1) ratio.

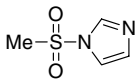
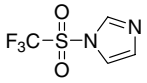
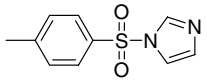
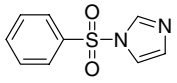
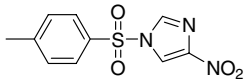
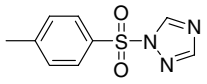
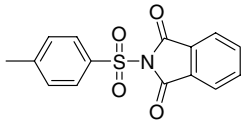
The optimized amount of TsIm was found to be 1.2–2.0 equiv per equivalent of alcohol. We also investigated other TsIm analogues (Table 4).

As the data in Table 4 indicate, using TsIm (Table 4, entry 3) increased the reaction rate and yield in comparison with other sulfonyl analogues. Replacing the tolyl group in TsIm with methyl, trifluoromethyl, and phenyl did not afford satisfactory results (Table 4, entries 1, 2, and 4). Furthermore, other azole analogues of TsIm were not as effective as imidazole (Table 4, entries 5 and 6). *N*-Tosyl phthalimide (Table 4, entry 7) was inactive for the conversion even after refluxing for 48 h.

Various sulfonyl chlorides were also examined instead of TsIm (Table 5) but lower yields of esters were observed.

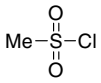
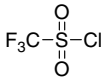
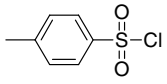
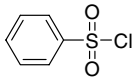
Using carboxylic acids instead of their sodium salts afforded lower yields of the corresponding esters (Scheme 1).[23] The generality and versatility of this method was demonstrated by its application to a wide range of structurally diverse alcohols and sodium carboxylate salts (Table 6). As the results in Table 6 indicate, this method is suitable for primary, secondary, and tertiary alcohols. Moreover, this method is applicable for aromatic, N-protected amino acids, and aliphatic sodium carboxylate salts. The

Table 4
Comparison of TsIm reactivity with analogues on the conversion of 2-phenylethanol into phenethyl benzoate

Entry	Reagent	Time (h)	Yield[a] (%)
1		7	54
2		7	58
3		3	94
4		7	64
5		10	54
6		10	58
7		48	NR[b]

[a] Isolated yield.
[b] No reaction.

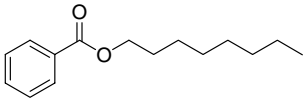
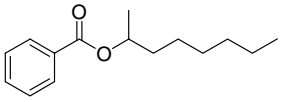
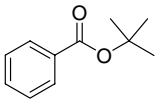
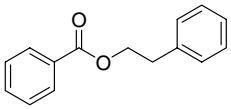
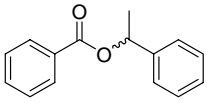
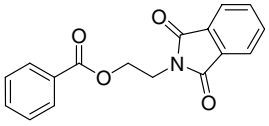
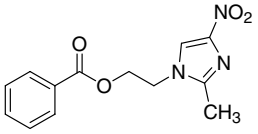
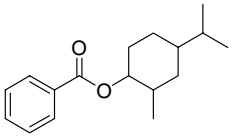
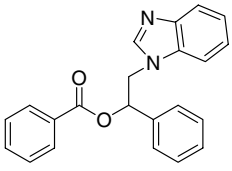
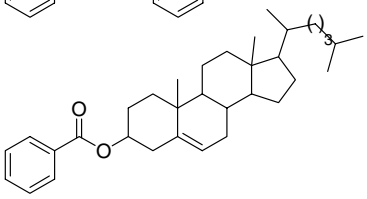
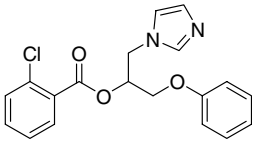
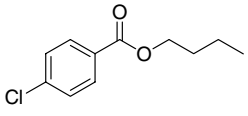
Table 5
Effect of various sulfonyl chlorides on the conversion of 2-phenylethanol into phenethyl benzoate

Entry	Sulfonyl chloride	Time (h)	Yield[a] (%)
1		8	42
2		8	48
3		8	50
4		8	37

[a] Isolated yield.

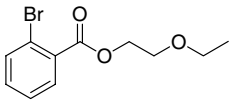
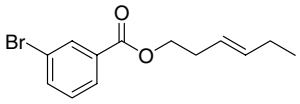
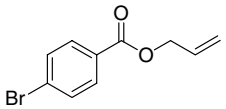
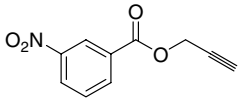
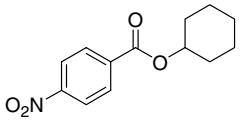
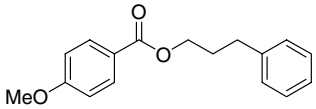
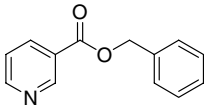
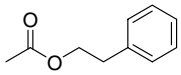
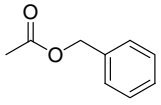
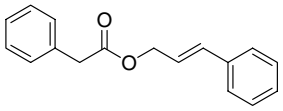
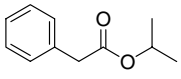
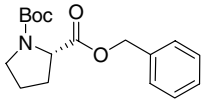
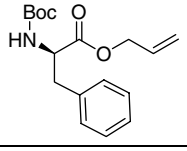
generality of the method was confirmed with respect to allylic (Table 6, entries 15 and 22), propargylic (Table 6, entry 16), benzylic (Table 6, entries 5, 9, 19, and 21), aliphatic (Table 6, entries 1–3, 12–14, and 23), alicyclic (Table 6, entries 8, 10, and 17) and other alcohols containing N-heterocycles (Table 6, entries 6, 7, 9, and 11).

Table 6
Esterification of alcohols with sodium carboxylates using TsIm/TBAI/TEA in refluxing DMF

Entry[Ref.]	Ester[a]	Time (h)	Yield[b] (%)
1[3b,26,27]		3	92
2[27b]		4	70
3[3a,28]		4	51
4[3b,29]		3	94
5[29]		4	65[c]
6		4	88
7		4	91
8		5	64
9		7	68
10[18a]		7	43
11		7	65
12[28a]		3	92

(continued on next page)

Table 6 (*continued*)

Entry[Ref.]	Ester[a]	Time (h)	Yield[b] (%)
13		4	84
14		4	88
15[30a]		3	92
16[30a]		4	90
17[3b,30b]		5	63
18[31a]		4	87
19[31b]		3	91
20[31c]		5	81
21[3c–e,21]		4	84
22		5	80
23[32]		5	61
24[33]		6	86
25[34]		7	82

[a] All products were characterized by ^{1}H and ^{13}C NMR, IR, CHN, and MS analysis.

[b] Isolated yield.

[c] Also obtained from optically pure *R*-(+)-1-phenylethanol, $[\alpha]_D^{20}$ +45 (*c* 5, in MeOH) in 52% ee.

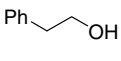
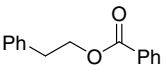
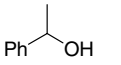
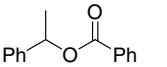
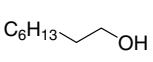
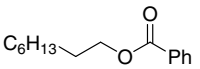
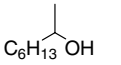
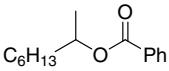
Furthermore, the benzoylation of cholesterol was possible using this method (Table 6, entry 10).

The selectivity of this method was demonstrated via a competitive reaction of a mixture consisting of 2-phenylethanol/1-phenylethanol/$PhCO_2Na$/TsIm in the molar ratio of (1:1:0.5:0.5) under the optimized conditions. The results in Table 7 demonstrate the selectivity between primary and secondary alcohols. There was high selectivity for esterification of the primary alcohol rather than the secondary analog. The same result was observed when a mixture of 1-octanol and 2-octanol was investigated (Table 7).

Mechanistically, it is assumed that esterification of the alcohol was achieved by a similar mechanism to that previously described for one-pot azidation[22a] and cyanidation[22b] of alcohols using TsIm.

Thus, the alcohol is first converted into an alkyl tosylate and subsequently via an S_N2 type reaction, the nucleophile (azide or cyanide) reacts with the alkyl tosylate to afford the product. However, there are several facts that confirm that the TsIm-mediated esterification reaction of the alcohol is not achieved merely via an S_N2 type reaction: (a) Full analysis of the reaction mixture revealed the presence of mixed anhydrides of carboxylic and sulfonic acids[24] besides alkyl tosylate (from the reaction of alcohol and TsIm). (b) Using our method for the conversion of optically pure *R*-(+)-1-phenylethanol into its corresponding ester (Table 6, entry 5) was accompanied by a reduction in optical purity (52% ee). This can be explained as a result of partial inversion resulting from an S_N2 type reaction of the carboxylate anion and the alkyl tosylate and retention of configuration from the reaction of mixed anhydrides and the alcohol at the same time. (c) Using quantum mechanical calculations including ab initio,[25] 6-31G or semi-empirical[25] Austin Model 1 (AM1) and Parameterized Model 3 (PM3) endorse the formation of mixed anhydrides in comparison with alkyl tosylates. Furthermore, frontier molecular orbital (FMO) theory[25] calculations have indicated better interaction of the carboxylate anion HOMO with the LUMO of

Table 7
Competitive esterification of primary/secondary ROH with $PhCO_2Na$ using TsIm

Entry	Alcohol mixture	Ester	Time (h)	Yield[a] (%)
1			3	96
				4
2			4	97
				3

[a] Isolated yield.

TsIm in comparison with interaction of the alcohol conjugate base HOMO and the LUMO of TsIm.

In conclusion, a convenient, efficient, and selective method has been established for the esterification of alcohols using TsIm/RCO_2Na/TEA/TBAI (cat.) in refluxing DMF. This method has favorable generality and applicability for various structurally diverse alcohols including primary, secondary, and tertiary alcohols with selectivity: $1° > 2° > 3°$.

General procedure for esterification of alcohols with sodium carboxylate using TsIm: To a double-necked round bottom flask (100 mL) equipped with a condenser was added a mixture of alcohol (0.01 mol), TsIm[22a] (0.012 mol), TEA (0.015 mol), RCO_2Na (0.02 mol) and a catalytic amount of TBAI (0.1 g) in DMF (30 mL). The mixture was refluxed, and in most cases, darkening occurred. Reflux was continued until TLC monitoring indicated no further improvement in the conversion (Table 6). The solvent was evaporated under vacuum and the remaining foam was dissolved in $CHCl_3$ (100 mL) and subsequently washed with water (2×100 mL). The organic layer was dried (Na_2SO_4) and evaporated. The crude product was purified by column chromatography on silica gel eluting with a mixture of *n*-hexane/EtOAc.[35]

Acknowledgments

We wish to thank the Shiraz University of Technology and Shiraz University Research Councils for partial support of this work. We are also grateful to Ms. L. Mehboudi for her assistance.

References and notes

1. (a) Otera, J. *Esterification: Methods, Reactions and Applications*; Wiley-VCH: Weinheim, 2006; (b) Larock, R. C. *Comprehensive Organic Transformations*, 2nd ed.; VCH: New York, 1999; p 1932.
2. (a) March, J. *Advanced Organic Chemistry*, 4th ed.; John Wiley & Sons (Asia) Ltd: Singapore, 2005; (b) Green, T. W.; Wuts, P. G. *Protective Groups in Organic Synthesis*, 3rd ed.; Wiley-Interscience: New York, 1999; p 372.
3. (a) Sato, T.; Otera, J.; Nozaki, H. *J. Org. Chem.* **1992**, *57*, 2166–2169; (b) McNulty, J.; Cheekoori, S.; Nair, J. J.; Larichev, V.; Capretta, A.; Robertson, A. J. *Tetrahedron Lett.* **2005**, *46*, 3641–3644; (c) Brinchi, L.; Germani, R.; Savalli, G. *Tetrahedron Lett.* **2003**, *44*, 6583–6585; (d) Brinchi, L.; Germani, R.; Savalli, G. *Tetrahedron Lett.* **2003**, *44*, 2027–2029; (e) Saegusa, T.; Murase, I.; Ito, Y. *J. Org. Chem.* **1973**, *38*, 1753–1755.
4. Liu, Z.; Chen, Z.-C.; Zheng, Q.-G. *Synthesis* **2004**, 33–36.
5. Khalafi-Nezhad, A.; Soltani Rad, M. N.; Khoshnood, A. *Synthesis* **2003**, 2552–2558.
6. Park, C. S.; Choi, H. G.; Lee, H.; Lee, W. K.; Ha, H.-J. *Tetrahedron: Asymmetry* **2000**, *11*, 3283–3292.
7. Pizey, J. S. In *Synthetic Reagents*; Wiley: New York, 1974; Vol. 2; pp 65–142.
8. Barry, J.; Bram, G.; Decodts, G.; Loupy, A.; Pigeon, P.; Sansoulet, J. *Tetrahedron* **1983**, *39*, 2673–2677.
9. Raber, D. J.; Gariano, P.; Brod, A. O., Jr.; Gariano, A.; Guida, W. C.; Guida, A. R.; Herbst, M. D. *J. Org. Chem.* **1979**, *44*, 1149–1154.
10. (a) Vorbrüggen, H. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 211–212; (b) Brechbühler, H.; Büchi, H.; Hatz, E.; Schreiber, J.; Eschenmoser, A. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 212–213.
11. Harris, M. M.; Patel, P. K. *Chem. Ind.* **1973**, *20*, 1002.
12. Szmuszkovicz, J. *Org. Prep. Proceed. Int.* **1972**, *4*, 51–53.
13. Fry, S. E.; Pienta, N. J. *J. Org. Chem.* **1984**, *49*, 4877–4880.
14. Derevitskaya, V. A.; Klimov, E. M.; Kochetkov, N. K. *Tetrahedron Lett.* **1970**, *11*, 4269–4270.
15. Curtis, V. A.; Schwartz, H. S.; Hartman, A. F.; Pick, R. M.; Kolar, L. W.; Baumgarten, R. J. *Tetrahedron Lett.* **1977**, *18*, 1969–1972.
16. (a) Wiberg, K. B.; Kass, S. R. *J. Am. Chem. Soc.* **1985**, *107*, 988–995; (b) Shi, M.; Xu, B. *Org. Lett.* **2002**, *4*, 2145–2148.
17. (a) Peterson, P. E.; Tao, E. V. P. *J. Org. Chem.* **1964**, *29*, 2322–2325; (b) Guenzet, J.; Camps, M. *Tetrahedron* **1974**, *30*, 849–856.
18. (a) Mitsunobu, O. *Synthesis* **1981**, 1–28; (b) Liobner, H.; Zbiral, E. *Helv. Chim. Acta* **1976**, *59*, 2100–2113.
19. Varasi, M.; Walker, K. A. M.; Maddox, M. L. *J. Org. Chem.* **1987**, *52*, 4235–4238.
20. Rollin, P. *Synth. Commun.* **1986**, *16*, 611–616.
21. Ramaiah, M. *J. Org. Chem.* **1985**, *50*, 4991–4993.
22. (a) Soltani Rad, M. N.; Behrouz, S.; Khalafi-Nezhad, A. *Tetrahedron Lett.* **2007**, *48*, 3445–3449; (b) Soltani Rad, M. N.; Khalafi-Nezhad, A.; Behrouz, S.; Faghihi, M. A. *Tetrahedron Lett.* **2007**, *48*, 6779–6784.
23. Similar reaction conditions were employed for carboxylic acid except that 3 equiv of TEA were employed.
24. Mazur, Y.; Karger, M. H. *J. Org. Chem.* **1971**, *36*, 528–531.
25. The ab initio (6-31G) quantum mechanic calculations were run using GAUSSIAN 98 version 9.2 software. The semi-empirical Austin Model 1 (AM1) and Parameterized Model 3 (PM3) calculations were run on MOPAC in CS Chem 3D Ultra 8(2004 Cambridge Soft) and Hyperchem (Hypercube Inc., version 7). HOMO and LUMO were indicated by Hyperchem (Hypercube Inc., version 7) software.
26. (a) Mori, N.; Togo, H. *Tetrahedron* **2005**, *61*, 5915–5925; (b) Ishihara, K.; Nakagawa, S.; Sakakura, A. *J. Am. Chem. Soc.* **2005**, *127*, 4168–4169.
27. (a) Mercs, L.; Pozzi, G.; Quici, S. *Tetrahedron Lett.* **2007**, *48*, 3053–3056; (b) Wakasugi, K.; Nakamura, A.; Tanabe, Y. *Tetrahedron Lett.* **2001**, *42*, 7427–7430.
28. (a) Yoo, W.-J.; Li, C.-J. *Tetrahedron Lett.* **2007**, *48*, 1033–1035; (b) Travis, B. R.; Sivakumar, M.; Hollist, G. O.; Borhan, B. *Org. Lett.* **2003**, *5*, 1031–1034.
29. Chen, C.-T.; Munot, Y. S. *J. Org. Chem.* **2005**, *70*, 8625–8627.
30. (a) Raj, I. V. P.; Sudalai, A. *Tetrahedron Lett.* **2005**, *46*, 8303–8306; (b) Elson, K. E.; Jenkins, I. D.; Loughlin, W. A. *Tetrahedron Lett.* **2004**, *45*, 2491–2493.
31. (a) Bergmeier, S. C.; Arason, K. M. *Tetrahedron Lett.* **2000**, *41*, 5799–5802; (b) Khan, K. M.; Maharvi, G. M.; Hayat, S.; Zia-Ullah; Choudhary, M. I.; Atta-ur-Rahman *Tetrahedron* **2003**, *59*, 5549–5554; (c) Reetz, M. T.; Wiesenhöfer, W. *Chem. Commun.* **2004**, 2750–2751.
32. Hwu, J. R.; Hsu, C.-Y.; Jain, M. L. *Tetrahedron Lett.* **2004**, *45*, 5151–5154.
33. Rodrigues, R. D. C.; Barros, I. M. A.; Lima, E. L. S. *Tetrahedron Lett.* **2005**, *46*, 5945–5947.
34. Saito, Y.; Watanabe, T.; Takahata, H. *Tetrahedron Lett.* **2006**, *47*, 3099–3102.
35. Selected data (Table 6, entries 7, 9 and 11). *Benzoic acid 2-(2-methyl-4-nitroimidazol-1-yl)ethyl ester* (Table 6, entry 7): pale yellow crystals; R_f (EtOAc/*n*-hexane) (2:1) 0.29; mp 137.4 °C; ^{1}H NMR ($CDCl_3$, 250 MHz): δ_{ppm} 2.38 (s, 3H, Me), 4.26 (*t*, 2H, $J = 5.3$ Hz, NCH_2), 4.53 (*t*, 2H, $J = 5.3$ Hz, OCH_2), 7.32–7.47 (m, 3H, aryl); 7.76 (s, 1H, C(5)–H, imidazole), 7.83–7.86 (m, 2H, aryl); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_{ppm} 13.08, 46.02, 62.69, 120.06, 128.66, 128.77, 129.50, 133.70, 145.14, 149.63, 165.87; IR (KBr) ν cm^{-1}: 1710.9 (C=O); MS (EI) [*m*/*z* (%)]: 275.09 (33.8); Anal. Calcd for $C_{13}H_{13}N_3O_4$: C, 56.72; H, 4.76; N, 15.27. Found: C, 56.77; H, 4.80; N, 15.20. *Benzoic acid 2-(benzimidazol-1-yl)-1-phenylethyl ester* (Table 6, entry 9): bright

yellow oil; R_f (EtOAc/*n*-hexane) (5:1) 0.56; ^{1}H NMR ($CDCl_3$, 250 MHz): δ_{ppm} 4.08 (dd, 1H, $J = 4.5$, 15.0 Hz, NCH_aH_b), 4.17 (dd, 1H, $J = 6.3$, 15.0 Hz, NCH_aH_b), 5.95 (*t*, 1H, $J = 4.9$ Hz, OCH), 6.82–7.00 (complex, 12H, aryl), 7.37 (s, 1H, C(2)–H benzimidazole), 7.47–7.59 (m, 2H, aryl); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_{ppm} 49.28, 74.25, 109.91, 119.99, 122.13, 122.93, 126.00, 128.17, 128.37, 128.68, 129.12, 129.49, 133.30, 133.91, 136.72, 143.18, 143.52, 165.04; IR (liquid film) ν cm^{-1}: 1720.4 (C═O); MS (EI) [*m*/*z* (%)]: 342.14 (36.4); Anal. Calcd for $C_{22}H_{18}N_2O_2$: C, 77.17; H, 5.30; N, 8.18. Found: C, 77.21; H, 5.32; N, 8.15. *2-Chlorobenzoic acid 2-(imidazol-1-yl)-1-phenoxymethylethyl ester* (Table 6, entry 11): bright brown oil; R_f (EtOAc/*n*-hexane) (5:1) 0.36; ^{1}H NMR ($CDCl_3$, 250 MHz): δ_{ppm} 3.71 (*d*, 2H, $J = 4.7$ Hz, NCH_2), 4.07 (d, 2H, $J = 4.7$ Hz, $PhOCH_2$), 5.23 (m, 1H, OCH), 6.54–6.95 (complex, 10H, C(4), C(5)–H imidazole, aryl), 7.32–7.35 (m, 1H, aryl), 7.41 (s, 1H, C(2)–H imidazole); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_{ppm} 46.72, 65.33, 71.49, 114.48, 120.09, 121.52, 126.78, 127.93, 129.10, 130.01, 130.40, 131.16, 131.30, 133.37, 137.65, 157.77, 164.30; IR (liquid film) ν cm^{-1}: 1726.2(C═O); MS (EI) [*m*/*z* (%)]: 356.09 (48.5); Anal. Calcd for $C_{19}H_{17}ClN_2O_3$: C, 63.96; H, 4.80; Cl, 9.94; N, 7.85. Found: C, 63.90; H, 4.83; Cl, 9.89; N, 7.88.