Nucleophilic Substitution Reactions of (Alkoxymethylene)dimethylammonium Chloride

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The use of imidate esters as potential replacements for diethyl azodicarboxylate and triphenylphosphine in the Mitsunobu reaction is described. A series of secondary alcohols were allowed to react with (chloromethylene)dimethylammonium chloride, generated from dimethylformamide (DMF) and oxalyl chloride, to give imidate esters. Reaction of these salts with potassium benzoate or potassium phthalimide gave the products of S_N2 substitution in excellent yields with clean inversion of stereochemistry. Optimization of reaction conditions is discussed as a means to increase the atom economy of the process by minimizing the quantity of nucleophile required.

Introduction

The conversion of secondary alcohols into esters with net inversion of configuration is a reaction of considerable importance in synthesis. The Mitsunobu reaction is the process *par excellence* for this transformation.[1,2] In this reaction, an alcohol is treated with triphenylphosphine and diethyl azodicarboxylate and a carboxylic acid to provide the target ester. The Mitsunobu reaction is applicable for a diverse array of secondary alcohols and has also been utilized in lactonization and macrolactonization reactions.[3] This reaction has been extended to a wide range of nucleophiles in addition to carboxylic acids to provide a variety of S_N2 substitution products. For example, the stereospecific preparation of amines from the corresponding alcohol can be effected via formation of the phthalimido derivative.[4] There are, however, disadvantages associated with the Mitsunobu reaction. Diethyl azodicarboxylate is unstable and potentially explosive, and the byproducts triphenylphosphine oxide and diethyl hydrazinedicarboxylate are of considerable mass, making the process nonideal from the point of view of atom economy.[5] Clearly, for large-scale applications, there is a need for a general alternative to the Mitsunobu reaction that is both safe and atom economic. Eschenmoser has reported the use of dimethylformamide (DMF) acetals in the esterifications of carboxylic acids.[6] These reactions proceed in good yields, with clean inversion of stereochemistry, but by necessity require two equivalents of alcohol and also suffer from restrictions with respect to the structure of the alcoholic component.

Recently, one of us reported the use of Vilsmeier chemistry to effect the stereospecific cyclization of hydroxyphenols **1** to provide dihydrobenzodioxans **3** via (alkoxymethylene)dimethylammonium salts **2** and intramolecular displacement by phenoxide (Scheme 1).[7] This methodology was subsequently extended to clean inversion with carboxylates[8] and phthalimide.[9]

The innocuous DMF and potassium chloride formed as side products in these reactions of imidate esters are easily removed, making this methodology more suitable for large-scale operations. Herein we report full details and extensions of this methodology for the formation of esters and phthalimide derivatives from alcohols with net inversion of stereochemistry.

Results and Discussion

Formation of Benzoate Esters with Inversion of Stereochemistry. The starting point for this investigation was an examination of the reaction of a series of secondary alcohols with (chloromethylene)dimethylammonium chloride, generated from DMF and oxalyl chloride,[10] to give the corresponding imidate esters. These were allowed to react with potassium benzoate in tetrahydrofuran (THF) to provide the benzoate esters **4**−**13** (Table 1).[8]

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† Department of Chemistry.
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(1) For reviews see: (a) Mitsunobu, O. *Synthesis* **1981**, 1; (b) Hughes, D. L. *Org. React.* **1992**, *42*, 335.

(2) For some recent applications see: (a) Castro, J. L.; Matassa, V. G. *J. Org. Chem.* **1994**, *59*, 2289; (b) Tsunoda, T.; Yamamiya, Y.; Kawamura, Y.; Ito, S. *Tetrahedron Lett.* **1995**, *36*, 2529.

(3) For recent examples see: (a) Rychnovsky, S. D.; Hwang, K. *J. Org. Chem.* **1994**, *59*, 5414; (b) Justus, K.; Steglich, W. *Tetrahedron Lett.* **1991**, *32*, 5781; (c) Barrett, A. G. M.; Carr, A. E.; Attwood, S. V.; Richardson, G.; Walshe, N. D. A. *J. Org. Chem.* **1986**, *51*, 4840.

(4) (a) Mitsunobu, O.; Wada, M.; Sano, T. *J. Am. Chem. Soc.* **1972**, *94*, 679; (b) Mulzer, J.; Funk, G. *Synthesis* **1995**, 101; (c) Mulzer, J.; Brand, C. *Tetrahedron* **1986**, *42*, 5961; (d) Simon, C.; Hosztafi, S.; Makleit, S. *Tetrahedron* **1994**, *50*, 9757; (e) Grunewald, G. L.; Paradkar, V. M.; Pazhenchevsky, B.; Pleiss, M. A.; Sall, D. J.; Seibel, W. L.; Reitz, T. J. *J. Org. Chem.* **1983**, *48*, 2321.

(5) For a review on atom economy see: Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 259.

(6) (a) Büchi, H.; Steen, K.; Eschenmoser, A. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 62; (b) Brechbuhler, H.; Büchi, H.; Hatz, E.; Schreiber, J.; Eschenmoser, A. *Helv. Chim. Acta* **1965**, *48*, 1746.

(7) (a) Procopiou, P. A.; Brodie, A. C.; Deal, M. J.; Hayman, D. F. *Tetrahedron Lett.* **1993**, *34*, 7483; (b) Procopiou, P. A.; Brodie, A. C.; Deal, M. J.; Hayman, D. F.; Smith, G. M. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2249.

(8) Barrett, A. G. M.; Koike, N.; Procopiou, P. A. *J. Chem. Soc., Chem. Commun.* **1995**, 1403.

(9) Barrett, A. G. M.; Braddock, D. C.; James, R. A.; Procopiou, P. A. *Chem. Commun.* **1997**, 433.

(10) Reichardt, C.; Schagerer, K. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 323.

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Scheme 1

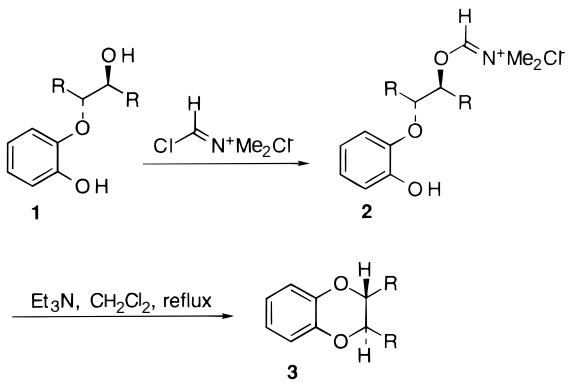
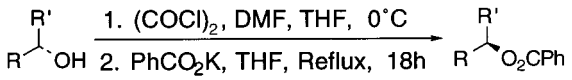
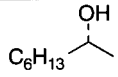
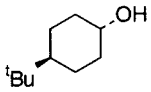
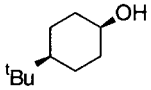
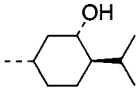
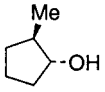
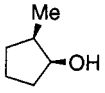
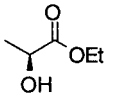
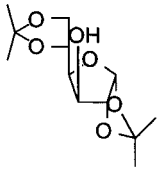


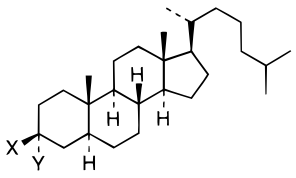
Table 1. Formation of Benzoate Esters with Inversion of Stereochemistry[a]



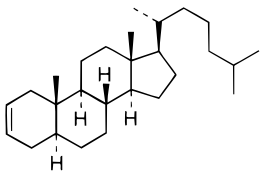
entry	alcohol	product	% yield	%ee/de	ref.
1		**4**	91	98[b]	24
2		**5**	73	97[c]	25
3		**6**	88	51[b]	26
4		**7**	64	97[d]	27
5		**8**	46	97[d]	27
6		**9**	70	95[d]	12
7		**10**	80	97[d,e]	-
8		**11**	74	97[d,e]	28
9		**12**	36	>95[b]	29
10		**13**	34	>95[c,f]	30

[a] All reactions performed with 5 equivalents of potassium benzoate [b] Determined by comparison of optical rotation with literature values. [c] Confirmed by comparison with authentic sample prepared from alcohol and benzoyl chloride in pyridine. [d] Diastereoselectivities determined by HPLC and ^{1}H NMR spectroscopy. [e] Racemic substrate employed. [f] Retention of configuration.

In all cases (with the exceptions of entries 3 and 10), the reactions were highly stereoselective and cleanly gave the products of S_N2 inversion. For 1−phenylethanol (entry 3), the reaction proceeded only with partial inversion (51% ee). It is reasonable to speculate that this example involved either a mixed S_N2/S_N1 reaction or took place in part via the corresponding benzylic chloride. In the case of entry 10, where **13** was obtained with complete retention of configuration (albeit in 34% yield), it can be assumed that the reaction took place via an S_N1 mechanism or through a competing pathway whereby benzoate reacts directly with the Vilsmeier reagent followed by transacylation as a result of steric hindrance in the alcoholic component.[11] THF was found to be a better solvent for the reactions than dichloromethane or DMF, as previously found for the Mitsunobu reaction.[12] In the case of DMF, the target esters were still obtained in good to excellent yields (80−95%), but with partial racemization having occurred. This partial loss of stereochemical integrity may be attributed to nucleophilic participation of the solvent (DMF) leading to inverted imidates or acceleration of substitution via the alkyl chloride. Inspection of the results in Table 1 reveals that this imidate methodology is applicable to a wide range of secondary alcohols. Furthermore, yields obtained from these imidate reactions compare very favorably with the Mitsunobu reaction. For example, sterically hindered menthol gives only a poor yield (20%) under Mitsunobu conditions,[12] although a 67% yield has been reported for a carefully conducted experiment,[11] compared with the 70% yield of inverted ester **9** obtained by reaction of the imidate. The reaction was extended to 5α-cholestan-3β-ol **14** and its 3α epimer **15**.[8] Thus, sterols **14** and **15** were smoothly converted into the 3α ester **16**[13] (65%) and 3β ester **17**[14] (53%), respectively. Although no elimination products were observed for the 3β sterol **14**, the 3α epimer **15**, which is set up favorably for *trans*-diaxial elimination, gave only small quantities (18%) of alkene **18**.

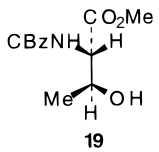


14 X = OH; Y = H
15 X = H; Y = OH
16 X = H; Y = O_2CPh
17 X = O_2CPh; Y = H

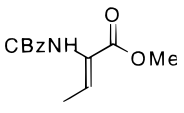


18

The threonine derivative **19** was explored as a potential "worst case" substrate because exposure of this alcohol to Mitsunobu conditions is known to give only the elimination product **20**.[15]



19

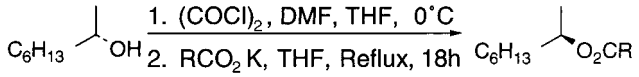


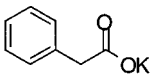
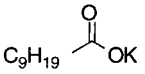
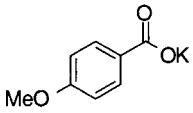
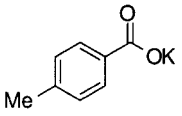
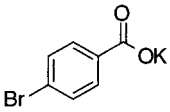
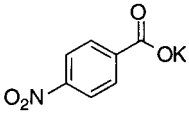
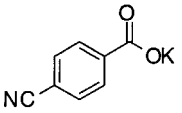
20

Disappointingly, reaction of the derived imidate with potassium benzoate under the standard conditions pro-

(11) For a discussion of the competing pathways in the Mitsunobu reaction and hence rational optimization of inverted ester yields see: Hughes, D. L.; Reamer, R. A. *J. Org. Chem.* **1996**, *61*, 2967.
(12) Dodge, J. A.; Trujillo, J. I.; Presnell, M. *J. Org. Chem.* **1994**, *59*, 234.
(13) Camp, D.; Jenkins, I. A. *Aust. J. Chem.* **1988**, *41*, 1835.

Table 2. Nucleophilic Inversion of 2-Octanol with a Range of Carboxylates[a]



entry	RCO_2K	product	% yield	Ref.
1		**21**	15	31
2		**22**	88[b]	32
3		**23**	79	33
4		**24**	69	34
5		**25**	54	35
6		**26**	31	33
7		**27**	27	

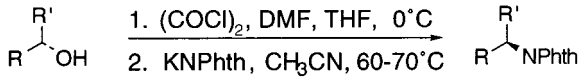
[a] All reactions performed with 5 equivalents of nucleophile. [b] Greater than 95% ee as determined by comparison with authentic sample prepared via Mitsunobu reaction of (*R*)-2-octanol.

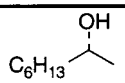
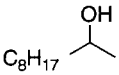
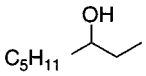
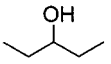
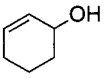
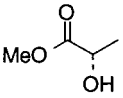
vided none of the desired S_N2 product, and crotonate **20**[16] was the major isolable product (60%).

Variation of Carboxylate Moiety; pK_a Dependence. With a view to variation of potassium benzoate as nucleophile, representative aliphatic carboxylic acids were examined. The substitution reactions of the imidate ester derived from 2-octanol with a variety of carboxylate salts were therefore explored yielding esters **21**−**27** (Table 2).

The use of sodium or potassium acetate as nucleophile proved unsuccessful, presumably due to the low solubility of sodium and potassium acetates in THF. The importance of anion solubility is apparent from the contrast between the lack of reaction observed with the acetates and the excellent yield of ester **22** obtained in the reaction of potassium decanoate (Table 2, entry 2). Moreover, a distinct correlation was observed in the reaction of substituted benzoates in which less acidic substrates (*p*-MeO and *p*-Me, entries 3 and 4) provide target esters **23** and **24** in substantially higher yields than those of **26** and **27** obtained with the more acidic substrates (*p*-NO_2 and *p*-CN, entries 6 and 7). In these cases, the mass balance was found to comprise of unreacted imidates (isolated as their formate esters after an aqueous work-up). Interestingly, this is in *direct contrast* to the trend observed in the Mitsunobu reaction in which higher yields are obtained with the more acidic substrates.[12]

Table 3. Formation of Phthalimido Derivatives with Inversion of Stereochemistry[a]



entry	alcohol	product[b]	% yield	%ee	ref.
1		**28**	95	96[c]	36
2		**29**	77	-[d]	
3		**30**	90	-[d]	
4		**31**	91	-	37
5		**32**	92	92[c]	38
6		**33**	73	72[c]	38
7		**34**	98	-[d]	39
8		**35**	34	-[d]	40
9		**36**	25	0[c]	41

[a] All reactions performed with 7 equivalents of potassium phthalimide in acetonitrile at 60−70 °C for 18 h. [b] NPhth = phthalimido derivative. [c] Determined by HPLC on a chiral stationary phase. [d] Racemic substrate employed.

Formation of Phthalimido Derivatives from Secondary Alcohols. Treatment of imidate esters derived from secondary alcohols with potassium phthalimide at 60−70 °C provide the phthalimide derivatives **28**−**36** with inversion of stereochemistry (Table 3).[9]

Clean inversion of stereochemistry was observed in the formation of representative phthalimido derivatives **28** and **32** (entries 1 and 5). We were pleased to find that no allylic rearrangement occurred in the substitution reaction of but-3-en-2-ol, and the phthalimido derivative **34** was isolated in excellent yield (entry 7). However, substitution of *(R)*-1-phenylethanol (entry 6) proceeded with partial racemization as previously observed in the esterification reaction for attempted substitution at benzylic positions (Table 1, entry 3). Several solvents were examined for these reactions of which acetonitrile was found to be superior. No reaction was observed in THF, whereas reaction in DMF or 1,2-dimethoxyethane DME gave the desired product in only moderate yield. Furthermore, the use of DMF as solvent led to partial racemization as was previously noted in the esterification reactions. The reaction of *(S)*-methyl lactate (entry 9) proceeded to give only a low yield of phthalimide derivative **36** with complete racemization having occurred.

In addition, the reaction of the imidate ester derived from 2-octanol with a variety of other nitrogen nucleophiles was investigated. The use of benzylamine and

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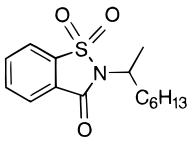
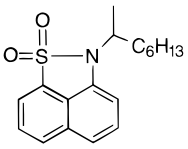
benzenesulfonamide salts proved unsuccessful, with none of the desired S_N2 products being isolated. However, utilization of the sodium salts of saccharin and 1,8-naphthosultam gave more encouraging results, and the target compounds **37** and **38** could be isolated in modest yields (62 and 34%, respectively). In these reactions, DME (reactions performed at 70 °C with 5 equivalents of nucleophile) was found to be a better solvent than THF, acetonitrile, or DMF.



37



38

Optimization of Reaction Conditions. In the work just described, all imidate reactions were carried out (by necessity) in the presence of a considerable excess of nucleophile. For example, all reaction with carboxylates utilized 5 equivalents of nucleophile, making these reactions nonideal from the point of view of atom economy. When the quantity of carboxylate was reduced, the yield of target ester fell and formation of alkyl chlorides predominated. For example, with 3 equivalents of potassium benzoate, 2-octyl benzoate **4** is formed in only a 48% yield compared with the 91% yield obtained when employing 5 equivalents (Table 1, entry 1). In the presence of 2 equivalents of nucleophile, only trace amounts of benzoate ester **4** could be detected. The observed chloride formation can be attributed to nucleophilic substitution by chloride ions present in the reaction medium.

To eliminate the possibility of alkyl chloride formation, the reaction of imidate esters with nonnucleophilic counterions was examined. A triflate counterion was incorporated into the imidate ester by formation of the Vilsmeier reagent from DMF and triflic anhydride.[17] Under the standard reaction conditions (THF, reflux, 16 h), considerable quantities of polymeric products, presumably derived from ring opening of THF, were isolated with only a small quantity (20%) of the desired ester being obtained. Addition of Hünig's base to remove traces of triflic acid from the reaction mixture failed to suppress the polymerization reaction, and attempts to repeat these reactions in alternative solvents (DMF, toluene, and 1,2-DCE) also proved unsuccessful.

A series of reactions of the imidate ester derived from 2-octanol were then performed to study the effects of variation in benzoate nucleophile and reaction conditions (Table 4). It was considered possible that the solubility of the benzoate nucleophile may be a limiting factor in these reactions. Attempts to increase the nucleophile solubility by carrying out reactions under sonification conditions[18] proved partially successful in that these reactions were found to proceed at 30 °C, a significantly lower temperature, and over a shorter reaction time (Table 4, entries 1 and 2). However, these reactions only provided satisfactory yields of ester in the presence of 5 equivalents of carboxylate.

(17) Martinez, A. G.; Alvarez, R. M.; Barcina, J. O.; de la Moya Cerero, S.; Vilar, E. T.; Fraile, A. G.; Hanack, M.; Subramanian, L. R. *J. Chem. Soc., Chem. Commun.* **1990**, 1571.

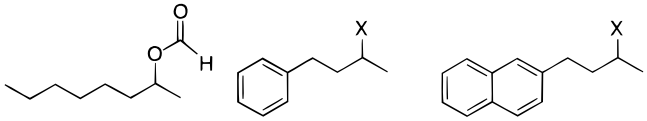
(18) Sonification conditions; Kerry Pulsatron bath for 4−6 h, ≈30 °C.

Table 4. Effect of Benzoate Counterion on Nucleophilic Attack on Imidate Derived from 2-Octanol

entry	M^+	X	conditions	%yield **4**
1	K^+	5	THF/sonification[a]	86
2	K^+	3	THF/sonification[a]	44
3	Bu_4N^+[b]	5	THF/reflux/16 h	0
4	Et_4N^+	5	THF/reflux/16 h	0
5	Et_3NH^+[c]	5	THF/reflux/16 h	88
6	Et_3NH^+[c]	3	THF/reflux/16 h	56
7	Ag^+	5	THF/reflux/16 h	96
8	Ag^+	3	THF/reflux/16 h	53
9	K^+	2	THF/reflux/16 h + Et_3N (2 eq)	31
10	K^+	2	THF/reflux/16 h + Hünig's base (2 eq)	53

[a] Kerry Pulsatron bath, 4−6 h, 30 °C. [b] Formed from silver benzoate and tetrabutylammonium iodide. [c] Generated in situ from triethylamine and benzoic acid (1:1 ratio).

The use of supposedly more soluble benzoate salts in place of potassium benzoate was then investigated. Reactions of tetrabutylammonium and tetraethylammonium benzoate (Table 4, entries 3 and 4) proved less successful than with potassium benzoate, and formate ester **39**[19] (presumably derived from hydrolysis on work up of unreacted imidate) was the major isolable product (typically 25−40%).



39

40 ; X = OH
41 ; X = $OCHNMe_2^+Cl^-$
42 ; X = O_2CPh
43 ; X = Cl

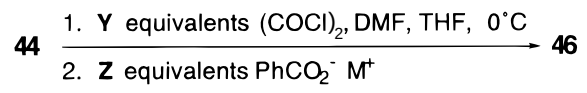
44 ; X = OH
45 ; X = $OCHNMe_2^+Cl^-$
46 ; X = O_2CPh
47 ; X = Cl

The use of a triethylammonium salt, generated by in situ reaction of triethylamine and benzoic acid gave more encouraging results as did the use of silver benzoate (entries 5 and 7), and the benzoate ester **4** could be isolated in excellent yields in the presence of 5 equivalents of nucleophile. However, in both these instances, the yield fell substantially when the number of equivalents of nucleophile was reduced to 3 equivalents (entries 6 and 8).

One equivalent of HCl is necessarily generated as a consequence of imidate formation, and this HCl should dispense with at least 1 equivalent of nucleophile via acid−base neutralization. Accordingly, a series of reactions were carried out in the presence of base. Tertiary nitrogen bases, such as triethylamine and Hünig's base, proved moderately successful and reasonable yields of benzoate ester **4** were isolated from runs with 2 equivalents of nucleophile (Table 4, entries 9 and 10). Surprisingly, incremental increases in base (2−20 equivalents of Hünig's base) led to a corresponding decrease in yield of ester as determined by semiquantitative HPLC experiments using the UV-active 4-phenylbutan-2-ol **40** as the substrate.

(19) Mori, K.; Kuwahara, S. *Tetrahedron* **1986**, *42*, 5539.

Table 5. Effect of Variation of Potassium Benzoate as a Function of Quantity of Vilsmeier Reagent



entry[a]	Y	Z	%yield **46**	%yield **47**	**44**[b]
1	1.15	5	86	11	–
2	1.15	4	62	37	–
3	1.15	2	0	88	–
4	1.00	5	69	3	23
5	1.00	4	70	4	21
6	1.00	3	70	4	–[c]
7	1.00	2	71	13	16
8	1.00	1	0	76	22
9	1.00	1	19[d]	68	3

[a] All runs performed at least twice. [b] Recovered alcohol. [c] Residual alcohol present but not isolated. [d] Two equivalents of Hünig's base added.

In the study of the reaction of imidate **41** derived from **40**, a 77% yield of benzoate ester **42**[20] was obtained under the standard conditions of 5 equivalents of potassium benzoate in refluxing THF. With 3 equivalents of potassium benzoate, ester **42** was obtained in a vastly reduced 30% yield and 41% of chloride **43**[21] was also isolated. These, and all the reactions already described were carried out utilizing a slight excess (1.15 equivalents) of the Vilsmeier reagent. The use of exactly 1.0 equivalent of Vilsmeier reagent in conjunction with just 3 equivalents of potasssium benzoate yielded ester **42** in an increased 63% yield with minimal chloride formation (<5%).

To investigate this effect further, a series of reactions were carried out using 4-(2-naphthyl)-butan-2-ol **44,** which was prepared via aldol condensation of 2-naphthaldehyde and acetone followed by reduction with lithium aluminum hydride. This alcohol was considered a suitable substrate because all possible side-products, such as the chloride **47** and alkenes, would be nonvolatile, allowing for quantitative isolation of all products. The S_N2 substitution of alcohol **44** was then carried out in the presence of either 1.15 or 1.00 equivalents Vilsmeier reagent and varying quantities of potassium benzoate as nucleophile (Table 5). Employing 1.15 equivalents of Vilsmeier reagent resulted in markedly reduced ester formation and a concomitant increase in alkyl chloride **47** as the number of equivalents of potassium benzoate was reduced from 5 to 2 (entries 1−3). Runs performed in the presence of exactly 1.0 equivalent of Vilsmeier reagent showed no decrease in yield of **46** as the number of equivalents of potassium benzoate was lowered from 5 to 2 and only small quantities of alkyl chloride **47** were isolated (entries 4−7). Thus, careful control of Vilsmeier stoichiometry allows for the use of two equivalents of nucleophile with little or no detriment to the overall isolated yield of inverted ester **46**. This remarkable difference in product distribution as a function of the quantity of the Vilsmeier reagent is unexpected and may be a manifestation of the heterogeneous nature of the reaction mixtures. When the displacement was attempted in the presence of only one equivalent of nucleophile (entry 8) no ester **46** was obtained, presumably because all the carboxylate salt is neutralized by HCl. Addition of 2 equivalents of Hünig's base to compensate was partially successful (entry 9) and a low yield of ester **46** was obtained. However, the major product in this reaction was the alkyl chloride **47**. Because it is reasonable to assume that nucleophilic attack by benzoate and chloride ions are competing processes, the fact that chloride **47** is the predominant product indicates that substitution with chloride occurs faster than substitution by the benzoate nucleophile under these conditions.

Conclusions

The imidate methodology in this paper should be of use as an alternative to the Mitsunobu reaction particularly for larger scale applications and especially because the side products are innocuous (DMF and potassium chloride). The method is mechanistically similar to the synthesis of glycosides[22] and benzyl, allyl, and *tert*-butyl esters via trichloroacetimidate activation.[23] The optimized reaction conditions enabling good yields of esters to be obtained in the presence of only 2 equivalents of nucleophile make this methodology preferable to the Mitsunobu reaction from the point of view of atom economy.

Experimental Section

General Information. Potassium benzoate, carboxylic acids, potassium phthalimide, and secondary alcohols were purchased from commercial sources and employed without further purification. All reactions were carried out under a nitrogen atmosphere in oven-dried glassware and using freshly distilled solvents. Chromatography was carried out on silica gel purchased from BDH (40−63 μm). Eluants are given in parentheses.

Representative Procedure for Reaction of Imidate Esters with Potassium Benzoate (Table 1). To a solution of DMF (1.3 mmol, 94 mg, 0.10 mL in CH_2Cl_2 (1 mL) under nitrogen at room temperature, oxalyl chloride (1.15 mmol, 145 mg, 0.10 mL) was added in a dropwise manner to form (chloromethylene)dimethylammonium chloride as a white solid. Stirring was continued for another 5 min, and the salt was suspended in THF (8 mL). 4-(2-Naphthyl)-2-butanol **44** (1.0 mmol, 200 mg) was added to form a homogeneous solution of the imidate ester **45**. Potassium benzoate (5 mmol, 0.80 g) was added, and the reaction mixture was heated to reflux for 16 h. The mixture was allowed to cool to room temperature, and the organic solution washed with water (3 × 10 mL), dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography (hexanes:EtOAc, 10:1; $R_f = 0.39$) gave the benzoate ester **46** as a colorless oil (267 mg, 86%); IR (neat) 3056, 2976, 2933, 1711, 1275, 1114 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 8.05 (m, 2H), 7.78 (m, 3H), 7.63 (s, 1H), 7.30−7.59 (m, 6H), 5.25 (m, 1H), 2.88 (m, 2H), 2.06 (m, 2H), 1.41 (d, $J = 6.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.2, 139.1, 133.7, 132.8, 132.1, 130.8, 129.6, 128.3, 128.0, 127.6, 127.4, 127.2, 126.4, 125.9, 125.2, 71.3, 37.3, 30.1, 20.2; high-resolution mass spectrometry (HRMS): Calcd for $C_{21}H_{20}O_2$ ($M^{+\bullet}$): 304.1463. Found: 304.1460.

(*S*)-2-Octyl benzoate (4).[24] $[\alpha]_D^{25} = +33.3°$ (*c* 1.5, CH_2Cl_2) [lit.[24] $[\alpha]_D^{25} = +38.9°$ (*c* 0.8, THF)]; ^1H NMR ($CDCl_3$, 270 MHz) δ 8.04 (d, $J = 7.7$ Hz, 2H), 7.54 (m, 1H), 7.45 (m, 2H), 5.25 (m, 1H), 1.70 (m, 1H), 1.60 (m, 1H), 1.27−1.42 (m, 11H), 0.87 (t, *J*

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= 6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.2, 132.7, 131.0, 129.5, 128.3, 71.7, 36.1, 31.8, 29.2, 25.4, 22.6, 20.1, 14.1.

(*R*)-3-Methyl-2-butyl benzoate (5).[25] $[\alpha]_D^{25} = -35.0°$ (*c* 0.7, CH_2Cl_2). (*S*)-3-Methyl-2-butyl benzoate prepared from (*S*)-3-methyl-butan-2-ol and benzoyl chloride in pyridine; $[\alpha]_D^{25} = +36.0°$ (*c* 0.8, CH_2Cl_2) [lit.[25] $[\alpha]_D^{25} = +41.1°$ (*c* 2.35, $CHCl_3$)]; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.07 (d, *J* = 7.0 Hz, 2H), 7.57 (m, 1H), 7.46 (t, *J* = 6.8 Hz, 2H), 5.01 (m, 1H), 1.92−1.98 (m, 1H), 1.31 (d, *J* = 6.4 Hz, 3H), 1.30 (d, *J* = 6.4 Hz, 3H), 1.02 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.2, 132.7, 131.0, 129.5, 128.3, 75.8, 32.9, 18.2, 18.0, 16.8.

(*S*)-1-Phenyl-1-ethyl benzoate (6).[26] $[\alpha]_D^{25} = +11.2°$ (*c* 3.0, EtOH) [lit.[26] $[\alpha]_D^{25} = +20.9°$ (*c* 2.78, EtOH)]; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.19 (d, *J* = 7.0 Hz, 2H), 7.30−7.64 (m, 8H), 6.25 (q, *J* = 6.6 Hz, 1H), 1.76 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.8, 141.9, 133.0, 130.7, 129.7, 128.7, 128.4, 128.0, 126.1, 73.0, 22.5.

***cis*-4-*tert*-Butylcyclohexyl benzoate (7).**[27] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.08 (d, *J* = 7.0 Hz, 2H), 7.57 (m, 1H), 7.47 (t, *J* = 7.5 Hz, 2H), 5.30 (m, 1H), 1.08−2.16 (m, 9H), 0.92 (s, 9H).

***trans*-4-*tert*-Butylcyclohexyl benzoate (8).**[27] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.06 (d, *J* = 7.5 Hz, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 2H), 4.89 (m, 1H), 0.98−2.23 (m, 9H), 0.89 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.1, 132.6, 131.0, 129.6, 128.2, 74.3, 47.2, 32.5, 32.2, 27.6, 25.2; *m*/*z* (CI^+; NH_3) 261 $(M+H)^+$, 278 $(M+NH_4)^+$. Anal. Calcd for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29. Found: C, 78.17; H, 9.05.

(1*R*, 2*R*, 5*S*)-2-*iso*-Propyl-5-methylcyclohexyl benzoate (9).[12] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.08 (d, *J* = 7.1 Hz, 2H), 7.56 (t, *J* = 7.0 Hz, 1H), 7.46 (m, 2H), 5.48 (m, 1H), 0.82−2.19 (m, 18H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.8, 132.7, 131.1, 129.6, 128.6, 71.7, 47.1, 39.3, 34.9, 29.4, 26.8, 25.5, 22.2, 21.0, 20.9.

***cis*-2-Methylcyclopentyl benzoate (10).** ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.06 (d, *J* = 7.5 Hz, 2H), 7.57 (t, *J* = 7.3 Hz, 1H), 7.46 (t, *J* = 7.4 Hz, 2H), 5.36 (m, 1H), 1.45−2.28 (m, 7H), 1.07 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.3, 132.7, 131.0, 129.5, 128.3, 79.5, 38.9, 32.5, 31.8, 22.4, 14.1; *m*/*z* (CI^+; NH_3) 205 $(M+H)^+$, 222 $(M+NH_4)^+$. Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.89. Found: C, 76.38; H, 7.64.

***trans*-2-Methylcyclopentyl benzoate (11).**[28] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.05 (d, *J* = 7.0 Hz, 2H), 7.57 (t, *J* = 7.3 Hz, 1H), 7.45 (t, *J* = 7.3 Hz, 2H), 4.96 (m, 1H), 1.21−2.29 (m, 7H), 1.08 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.5, 132.7, 130.9, 129.5, 128.3, 83.2, 40.1, 32.0, 31.5, 22.6, 18.3.

(*R*)-Ethyl-2-(Benzoyloxy)propanoate (12).[29] $[\alpha]_D^{25} = -13.8°$ (*c* 1.0, $CHCl_3$) [lit.[29] (*S*)-**12** $[\alpha]_D^{25} = +13.6°$ (*c* 3.5, $CHCl_3$)]; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 8.09 (dd, *J* = 8.0, 1.0 Hz, 2H), 7.58 (m, 1H), 7.45 (m, 2H), 5.31 (q, *J* = 7.0 Hz, 1H), 4.23 (q, *J* = 7.0 Hz, 2H), 1.62 (d, *J* = 7.0 Hz, 3H), 1.27 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 172.3, 147.5, 134.8, 131.3, 131.0, 129.0, 70.7, 62.9, 18.6, 15.6.

3-*O*-Benzoyl-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (13).[30] $[\alpha]_D^{25} = -55.0°$ (*c* 1.0, $CHCl_3$) [lit.[30] $[\alpha]_D^{25} = -26.2°$ (*c* 1.0, EtOH); authentic 3-*O*-benzoyl-1,2;5.6-di-*O*-isopropylidene-α-D-glucofuranose prepared from benzoyl chloride and 1,2;5.6-di-*O*-isopropylidene-α-D-glucofuranose in pyridine; $[\alpha]_D^{25} = -53.5°$ (*c* 1.6, $CHCl_3$)]; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.03 (d, *J* = 8.0 Hz, 2H), 7.59 (t, *J* = 8.0 Hz, 1H), 7.45 (t, *J* = 8.0 Hz, 2H), 5.94 (d, *J* = 3.5 Hz, 1H), 5.50 (d, *J* = 3.0 Hz, 1H), 4.63 (d, *J* = 3.5 Hz, 1H), 4.35 (m, 2H), 4.10 (m, 2H), 1.55 (s, 3H), 1.41 (s, 3H), 1.32 (s, 3H), 1.26 (s, 3H).

5α-Cholestanyl-3α-benzoate (16).[13] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.09 (d, *J* = 6.2 Hz, 2H), 7.57 (t, *J* = 6.4 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 2H), 5.30 (br s, 1H), 0.86−2.07 (m, 44 H), 0.68 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.9, 132.7, 131.3, 129.6, 128.3, 70.8, 56.6, 56.4, 54.4, 42.6, 40.5, 40.1, 39.6, 36.2, 35.9, 35.9, 35.5, 33.3, 33.1, 32.0, 28.5, 28.3, 28.0, 26.4, 24.2, 23.9, 22.9, 22.6, 20.9, 18.7, 12.1, 11.5.

5α-Cholestanyl-3β-benzoate (17).[14] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.05 (d, *J* = 7.1 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.2 Hz, 2H), 4.97 (m, 1H), 0.88−2.02 (m, 44H), 0.68 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.1, 132.6, 131.0, 129.5, 128.2, 74.4, 56.5, 56.3, 54.3, 44.8, 42.6, 40.0, 39.6, 36.9, 36.2, 35.8, 35.6, 34.2, 32.0, 28.7, 28.3, 28.0, 27.6, 24.3, 23.9, 22.9, 22.6, 21.3, 18.7, 12.3, 12.1.

(*Z*)-2-(Benzyloxycarbonyl)amino-2-butenoic acid (20).[16] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.30−7.40 (m, 5H), 6.72 (q, *J* = 7.4 Hz, 1H), 6.15 (br s, 1H), 5.15 (s, 2H), 3.75 (s, 3H), 1.81 (d, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.0, 153.9, 136.0, 133.4, 128.6, 128.3, 128.2, 126.3, 67.4, 52.4, 14.3.

Representative Procedure for Reaction of Carboxylates with Imidate Ester Derived from 2-Octanol (Table 2). To a suspension of KH (10 mmol, 0.40 g) in THF (5 mL), a solution of 4-nitrobenzoic acid (10 mmol, 1.67 g) in THF (10 mL) was added gradually. The reaction mixture was stirred until evolution of hydrogen gas ceased. Separately, oxalyl chloride (2.30 mmol, 0.20 mL) was added in a dropwise manner with stirring to DMF (2.58 mmol, 0.20 mL) in CH_2Cl_2 (2 mL) to form (chloromethylene)dimethylammonium chloride as a white solid. This salt was suspended in THF (10 mL), and 2-octanol (2.0 mmol, 0.32 mL) added. This homogeneous solution was added to the suspension of the carboxylate salt, and the reaction mixture heated to reflux overnight. The mixture was cooled, filtered through Celite, concentrated under reduced pressure, and chromatographed (hexanes: EtOAc 20: 1, $R_f = 0.26$) to give 2-octyl 4-nitrobenzoate **26**[31] as a colorless oil (0.087 g, 31%); IR (neat) 3112, 2954, 2931, 2859, 1723, 1529, 1279 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 8.27 (d, *J* = 9 Hz, 2H), 8.19 (d, *J* = 9 Hz, 2H), 5.18 (m, 1H), 1.72 (m, 1H), 1.63 (m, 1H), 1.20−1.61 (m, 11H), 0.87 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.3, 150.5, 136.3, 130.6, 123.5, 73.2, 35.9, 31.7, 29.1, 25.4, 22.6, 20.0, 14.0; HRMS: Calcd for $C_{15}H_{21}NO_4$ ($M^{+\bullet}$): 279.1471. Found: 279.1471.

2-Octyl Phenylacetate (21).[32] ^{1}H NMR ($CDCl_3$, 270 MHz) δ 7.33 (m, 5H), 4.90 (m, 1H), 3.59 (s, 2H), 1.27−1.50 (m, 2H), 1.19−1.24 (m, 11H), 0.86 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.3, 134.4, 129.2, 128.5, 126.9, 71.6, 41.9, 35.9, 31.7, 29.1, 25.2, 22.5, 19.9, 14.1.

2-Octyl Decanoate (22).[33] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.89 (m, 1H), 2.27 (t, *J* = 7.4 Hz, 2H), 1.50−1.68 (m, 2H), 1.28−1.48 (m, 22H), 1.20 (d, *J* = 6.3 Hz, 3H), 0.88 (t, *J* = 6.3 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.6, 70.7, 36.0, 35.6, 34.8, 31.9, 31.8, 29.5, 29.3, 29.2, 25.4, 25.1, 22.7, 22.6, 20.0, 19.7, 14.1.

2-Octyl *p*-Methoxybenzoate (23).[31] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.00 (d, *J* = 8.9 Hz, 2H), 6.92 (d, *J* = 8.9 Hz, 2H), 5.13 (m, 1H), 3.87 (s, 3H), 1.62 (m, 2H), 1.29−1.42 (m, 11H), 0.89 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.0, 163.2, 131.5, 123.5, 113.5, 71.4, 55.4, 36.1, 31.8, 29.2, 25.4, 22.6, 20.1, 14.1.

2-Octyl *p*-Methylbenzoate (24).[34] ^{1}H NMR ($CDCl_3$, 250 MHz) δ 7.93 (d, *J* = 8.0 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 5.13 (m, 1H), 2.40 (s, 3H), 1.55−1.82 (m, 2H), 1.21−1.41 (m, 11H), 0.87 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 166.2, 143.2, 129.5, 128.9, 128.2, 71.4, 36.0, 31.7, 29.0, 25.3, 22.5, 21.6, 20.0, 14.0.

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2-Octyl *p*-Bromobenzoate (25).[35] ^{1}H NMR ($CDCl_3$, 270 MHz) δ 7.88 (d, J = 8.7 Hz, 2H), 7.56 (d, J = 8.7 Hz, 2H), 5.14 (m, 1H), 1.50−1.90 (m, 2H), 1.19−1.39 (m, 11H), 0.87 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.5, 131.6, 131.1, 129.8, 127.8, 72.16, 36.0, 31.7, 29.2, 25.4, 22.6, 20.1, 14.1.

2-Octyl *p*-Cyanobenzoate (27). IR (neat) 2955, 2929, 2858, 2231, 1714, 1277, 1106 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 8.14 (d, J = 8.0 Hz, 2H), 7.73 (d, J = 8.0 Hz, 2H), 5.17 (m, 1H), 1.55−1.82 (m, 2H), 1.21−1.43 (m, 11H), 0.87 (t, J = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 164.5, 134.7, 132.0, 130.0, 118.0, 116.1, 72.9, 35.9, 31.6, 29.0, 25.3, 22.5, 19.9, 14.0; HRMS: Calcd for $C_{16}H_{21}NO_2$ [$(M+NH_4)^{+\bullet}$]: 277.1916. Found: 277.1912.

Representative Procedure for Reaction of Imidate Esters with Potassium Phthalimide (Table 3). To a solution of DMF (1.29 mmol, 0.094 g, 0.10 mL) in CH_2Cl_2 (1 mL) under nitrogen at room temperature, oxalyl chloride (1.15 mmol, 0.145 g, 0.10 mL) was added in a dropwise manner to form (chloromethylene)dimethylammonium chloride as a white solid. Stirring was continued for another 5 min, and the salt was suspended in MeCN (20 mL) when 3-octanol (1.0 mmol, 0.130 g, 0.16 mL) and potassium phthalimide (7.0 mmol, 1.30 g) were added sequentially. The reaction mixture was heated to 65 °C for 16 h, cooled, and filtered through Celite. The residue, after evaporation, was chromatographed (EtOAc: hexanes, 1:20, R_f = 0.23) to provide *N*-(3-octyl)phthalimide **30** as a colorless oil (0.211 g, 90%); IR (neat) 2960, 2931, 2859, 1770, 1710, 1466, 1369, 1062 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.83 (m, 2H), 7.72 (m, 2H), 4.12 (m, 1H), 2.06 (m, 2H), 1.82 (m, 2H), 1.26 (m, 6H), 0.86 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 168.9, 133.8, 131.9, 123.1, 54.0, 32.2, 31.5, 26.4, 25.6, 22.5, 14.0, 11.1; HRMS: Calcd for $C_{16}H_{21}NO_2$ ($M^{+\bullet}$): 259.1572. Found 259.1583.

***(S)*-*N*-(2-Octyl)phthalimide (28).**[36] $[\alpha]_D^{25}$ = +14.0° (*c* 1.1, $CHCl_3$) [lit.[36] $[\alpha]_D^{25}$ = +15.2° (*c* 4.1, EtOH)]; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.82 (m, 2H), 7.70 (m, 2H), 4.34 (m, 1H), 2.06 (m, 1H), 1.69−1.79 (m, 1H), 1.46 (d, J = 6.9 Hz, 3H), 1.24−1.36 (m, 8H), 0.85 (t, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 168.6, 133.8, 132.0, 123.0, 47.5, 33.8, 31.7, 28.9, 26.8, 22.6, 18.7, 14.0.

***N*-(2-Decyl)phthalimide (29).** IR (neat) 2926, 2856, 1774, 1710, 1467, 1367 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.82 (m, 2H), 7.70 (m, 2H), 4.34 (m, 1H), 2.05 (m, 1H), 1.74 (m, 1H), 1.47 (d, J = 6.9 Hz, 3H), 1.24 (m, 12H), 0.84 (t, J = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz); δ 168.6, 133.8, 132.1, 123.0, 47.5, 33.7, 31.8, 29.4, 29.2, 29.2, 19.2, 26.8, 22.6, 18.7, 14.1; HRMS: Calcd for $C_{18}H_{25}NO_2$ ($M^{+\bullet}$) 287.1885. Found: 287.1873;

***N*-(3-Pentyl)phthalimide (31).**[37] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.82 (m, 2H), 7.71 (m, 2H), 4.04 (m, 1H), 2.05 (m, 2H), 1.78 (m, 2H), 0.87 (t, J = 7.4 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 168.8, 133.8, 131.8, 123.0, 55.6, 25.3, 11.1.

***(R)*-*N*-(2-Butyl)phthalimide (32).**[38] $[\alpha]_D^{25}$ = −12.8° (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 7.79 (m, 2H), 7.67 (m, 2H), 4.24 (m, 1H), 2.02 (m, 1H), 1.77 (m, 1H), 1.44 (d, J = 6.9 Hz, 3H), 0.86 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 168.6, 133.8, 132.1, 123.0, 49.1, 26.9, 18.4, 11.2.

***(S)*-*N*-((1-Phenyl)-1-ethyl)phthalimide (33).**[38] $[\alpha]_D^{25}$ = −31.4° (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 7.78 (m, 2H), 7.68 (m, 2H), 7.47−7.53 (m, 2H), 7.22−7.36 (m, 3H), 5.57 (q, J = 7.4 Hz, 1H), 1.93 (d, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 168.2, 140.4, 133.9, 132.0, 128.5, 127.7, 127.5, 123.2, 49.7, 17.6.

***N*-(2-Buten-3-yl)phthalimide (34).**[39] ^{1}H NMR ($CDCl_3$, 270 MHz) δ 7.81 (m, 2H), 7.69 (m, 2H), 6.18 (m, 1H), 5.20 (m, 2H), 4.91 (m, 1H), 1.57 (d, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 167.9, 136.9, 133.9, 132.1, 123.1, 116.3, 49.0, 18.2.

***N*-(Cyclohexen-2-yl)phthalimide (35).**[40] ^{1}H NMR ($CDCl_3$, 270 MHz) δ 7.84 (m, 2H), 7.70 (m, 2H), 5.96 (m, 1H), 5.58 (m, 1H), 4.92 (m, 1H), 1.67−2.27 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 168.2, 133.9, 132.1, 130.1, 126.6, 123.1, 47.5, 27.1, 24.3, 21.8.

Methyl 2-(*N*-Phthalimido)propanoate (36).[41] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.86 (m, 2H), 7.74 (m, 2H), 4.98 (q, J = 7.3 Hz, 1H), 3.74 (s, 3H), 1.69 (d, J = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.2, 167.4, 134.2, 131.9, 123.5, 52.8, 47.4, 15.3.

Procedure for Formation of *N*-(2-Octyl)saccharine (37). To a suspension of NaH (5.0 mmol, 0.12 g) in THF (5 mL), a solution of saccharin (5.0 mmol, 0.91 g) in THF (10 mL) was gradually added. The mixture was stirred for 1 h, and the solvent was removed under reduced pressure to provide the sodium salt of saccharin as a white solid. Separately, oxalyl chloride (1.15 mmol, 0.10 mL) was gradually added to a solution of DMF (1.29 mmol, 0.10 mL) in CH_2Cl_2 (1 mL) to form (chloromethylene)dimethylammonium chloride as a white solid. This solid was suspended in DME (15 mL), and 2-octanol (1.0 mmol, 0.13 g, 0.16 mL) was added to form a homogeneous solution that was added to the sodium saccharin salt, and the mixture was heated to 70 °C overnight. The reaction mixture was cooled, filtered through Celite, concentrated under reduced pressure, and chromatographed (hexanes:EtOAc, 20:1) to give the product **37** as a colorless oil (0.183 g, 62%); IR (neat) 2929, 2859, 1726, 1460, 1335, 1294, 1253, 1182 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.05 (m, 1H), 7.86 (m, 3H), 4.30 (m, 1H), 2.19 (m, 1H), 1.85 (m, 1H), 1.60 (d, J = 6.9 Hz, 3H), 1.28−1.37 (m, 8H), 0.88 (t, J = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 158.9, 137.8, 134.5, 134.2, 127.5, 125.0, 120.7, 51.5, 34.0, 31.7, 28.9, 26.7, 22.6, 18.8, 14.1; Anal. Calcd for $C_{15}H_{21}NO_3S$: C, 60.99; H, 7.17; N, 4.74. Found: C, 61.22; H, 7.07; N, 4.78.

***N*-(2-Octyl)-1,8-naphthosultam (38).** IR ($CHCl_3$) 2932, 2859, 1590, 1460, 1378, 1312, 1178, 1136 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.06 (d, J = 8.1 Hz, 1H), 7.96 (d, J = 7.1 Hz, 1H), 7.75 (m, 1H), 7.53 (m, 2H), 6.84 (d, J = 7.2 Hz, 1H), 4.31 (m, J = 6.9 Hz, 1H), 2.15 (m, 1H), 1.90 (m, 1H), 1.60 (d, J = 6.9 Hz, 3H), 1.23−1.42 (m, 8H), 0.87 (t, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 135.0, 131.1, 130.9, 130.5, 129.2, 127.9, 119.5, 119.4, 117.7, 104.4, 51.2, 34.2, 31.7, 29.0, 26.9, 22.6, 18.2, 14.1; *m/z* (CI^+; NH_3) 318 $(M+H)^{+\bullet}$, 335 $(M+NH_4)^+$; Anal. Calcd for $C_{18}H_{23}NO_2S$: C, 68.11; H, 7.31; N, 4.42. Found: C, 67.92; H, 7.54; N, 4.41.

2-Octyl Formate (39).[19] ^{1}H NMR ($CDCl_3$, 270 MHz) δ 8.03 (s, 1H), 5.00 (m, 1H), 1.48−1.56 (m, 2H), 1.17−1.34 (m, 11H), 0.87 (t, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 160.9, 71.1, 35.8, 31.7, 29.0, 25.3, 22.6, 20.0, 14.0.

2-(4-Phenyl)butyl Benzoate (42).[20] ^{1}H NMR ($CDCl_3$, 250 MHz) δ 8.05 (d, J = 8.0 Hz, 2H), 7.39−7.60 (m, 3H), 7.13−7.29 (m, 5H), 5.18 (m, 1H), 2.75 (m, 2H), 1.87−2.18 (m, 2H), 1.47 (d, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.2, 141.5, 132.8, 130.8, 129.5, 128.4, 128.3, 125.9, 71.2, 37.8, 31.8, 20.1.

4-Phenyl-2-chlorobutane (43).[21] ^{1}H NMR ($CDCl_3$, 250 MHz) δ 7.15−7.35 (m, 5H), 3.99 (m, 1H), 2.68−2.94 (m, 2H), 2.00 (m, 2H), 1.53 (d, J = 7.0 Hz, 3H).

4-(2-Naphthyl)-2-butanol (44). IR ($CHCl_3$) 3358, 3052, 2967, 2931, 1599 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.82 (m, 3H), 7.67 (br s, 1H), 7.47 (m, 2H),7.38 (d, J = 8.4 Hz, 1H), 3.89 (m, 1H), 2.91 (m, 2H), 1.90 (m, 1H), 1.28 (d, J = 6.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 139.6, 133.7, 132.0, 128.0, 127.6, 127.4, 127.3, 126.4, 126.0, 125.2, 67.53, 40.7, 32.3, 23.7; HRMS calcd for $C_{14}H_{16}O$ ($M^{+\bullet}$) 218.1544, found 218.1542.

4-(2-Naphthyl)-2-chlorobutane (47). IR (neat) 3052, 2970, 2926, 1600, 1508, 1445, 1378 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 7.81 (m, 3H) 7.67 (s, 1H), 7.34−7.48 (m, 3H), 4.00 (m,

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J = 5.8 Hz, 1H), 3.00 (m, 2H), 2.12 (m, 2H), 1.56 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.6, 133.7, 132.1, 128.1, 127.7, 127.5, 127.3, 126.7, 126.1, 125.3, 57.9, 41.8, 33.1, 22.5; HRMS calcd for $C_{14}H_{15}{}^{35}Cl$ ($M^{+\bullet}$) 218.0862, found 218.0862.

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Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra of **27**, **29**, **30**, **44**, **46,** and **47** (12 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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