ARTICLE

OBC
www.rsc.org/obc

The Hendrickson reagent and the Mitsunobu reaction: a mechanistic study †

Kathryn E. Elson,[a] Ian D. Jenkins*[b] and Wendy A. Loughlin[a]
[a] *School of Science, Griffith University, Nathan, Brisbane, QLD, 4111, Australia*
[b] *Natural Product Discovery, Griffith University, Nathan, QLD, 4111, Australia. E-mail: I.Jenkins@griffith.edu.au*

Received 14th May 2003, Accepted 25th June 2003
First published as an Advance Article on the web 15th July 2003

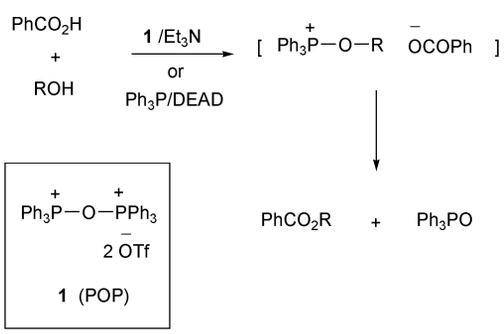
The alkoxytriphenylphosphonium ion intermediate of the Mitsunobu reaction can be generated using the Hendrickson reagent, triphenylphosphonium anhydride trifluoromethanesulfonate, **1**. Strangely, while the reagent **1** can be used in place of the Mitsunobu reagents (triphenylphosphine and a dialkylazodicarboxylate) for the esterification of primary alcohols, secondary alcohols such as menthol undergo elimination. Evidence is presented to show that this unexpected result is due to the presence of trialkylammonium triflate salts. Such salts lead to a dramatic decrease in the rate of esterification relative to competing elimination. The Mitsunobu esterification of menthol with *p*-nitrobenzoic acid was re-examined and the occurrence of elimination reported for the first time. The presence of traces of tetrabutylammonium triflate led to a dramatic reduction in the yield of inverted ester and a corresponding increase in the yield of *anti* elimination product 2-menthene. The mechanism of the Mitsunobu reaction is discussed in the light of the dramatic salt effect on both the rate and outcome of the reaction and the possible involvement of ion pair clustering. In contrast, use of the reagent **1** resulted in *syn* elimination to give a 1 : 2 mixture of 2- and 3-menthenes. Finally, **1** and sodium azide can be used to convert a primary alcohol into an azide in high yield. There was no reaction under Mitsunobu conditions.

Introduction

The Mitsunobu reaction[1–4] is one of the most useful and versatile reactions in organic synthesis. The beauty of the reaction lies in its generality and the mild reaction conditions employed. It enables the synthetic organic chemist to convert a primary or secondary alcohol into an excellent leaving group which can subsequently be displaced by a wide range of nucleophiles, either inter- or intra-molecularly. The one thousand or so references to the Mitsunobu reaction testify to its generality and usefulness.

In seeking an alternative protocol for the Mitsunobu reaction that avoided the use of dialkyl azodicarboxylates, we examined the Hendrickson "POP" reagent **1**.[5,6] This reagent, triphenylphosphonium anhydride trifluoromethanesulfonate, was discovered over 20 years ago, and appears to bring about dehydrations (ester, amide formation *etc*.) in a manner analogous to the Mitsunobu reaction. Indeed, the same key intermediate (an alkoxyphosphonium salt) is almost certainly involved in both reactions (Scheme 1).

Surprisingly, the similarity between the two reactions appears to have gone largely unnoticed although it was mentioned in an early paper by Ramos and Rosen[7] and in more recent papers by Hendrickson *et al*.[5,8] In contrast to the Mitsunobu reaction that is widely used, the Hendrickson reagent has been used only occasionally and as far as we are aware, has not been investigated as a means for inverting the configuration of an alcohol (a common use for the Mitsunobu reaction).



Scheme 1

Some advantages of the Hendrickson reagent over the Mitsunobu reagents are: (a) the recovered phosphine oxide can be readily recycled by treatment with trifluoromethanesulfonic anhydride (Tf_2O); (b) azodicarboxylates are not required; (c) competing Mitsunobu-type side reactions such as alkylation of the hydrazinedicarboxylate are eliminated. One disadvantage with using the reagent **1**, is that *two* moles of triphenylphosphine oxide are liberated per dehydration reaction [*e.g.*, eqn. (1)] compared with only one mole in the Mitsunobu reaction. This exacerbates the problem of separation of the product from triphenylphosphine oxide by chromatography. However, Hendrickson has reported the use of a POP reagent containing a basic group to facilitate removal of the phosphine oxide.[6a,b] A similar strategy has been employed in the Mitsunobu reaction.[9]

The reagent **1** sometimes gives a reaction where the Mitsunobu reaction fails. For example, alcohols can be reduced to alkanes with $NaBH_4$ (*via* alkoxyphosphonium salt formation with **1**) but not under Mitsunobu conditions.[8] We also investigated the latter reaction some years ago and observed only low yields of toluene from benzyl alcohol after addition of triphenylphosphine/diisopropyl azodicarboxylate (TPP/DIAD), followed by Super Hydride-$LiEt_3AlH$.[10] This difference in reactivity is possibly related to the presence of phosphoranes that are formed under Mitsunobu conditions.[11–13] In a more recent example, Hendrickson has shown that heating epoxides

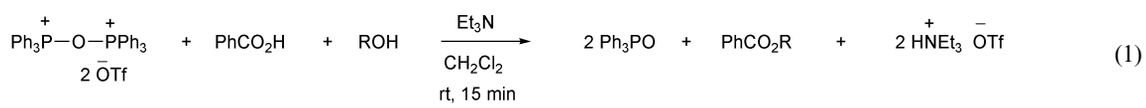
† Electronic supplementary information (ESI) available: (1) ^1H and ^{13}C NMR spectra of 4-chlorobenzyl thioacetate **3** and 4-chlorobenzyl azide **4**. (2) ^1H NMR stack spectra of alkene region of menthenes **5a**–**5b** formed by (a) thermolysis of menthol diphenylphosphate ester;[21] (b) Mitsunobu reagents (Organic Syntheses conditions);[16] (c) Hendrickson reagent (Table 1, entry 3) and (d) Hendrickson reagent (Table 1, entry 8). (3) ^{31}P spectra of Mitsunobu reactions performed in the presence of (a) diisopropylethylammonium triflate; (b) diisopropylethylammonium triflate and diisopropylethylamine (2 eq.) and (c) tetrabutylammonium triflate. (4) ^1H and $^1H\{^{31}P\}$ NMR spectra of (−)-menthoxytriphenylphosphonium triflate **11**, H3. (5) Table 2 – raw data for Fig. 3. See http://www.rsc.org/suppdata/ob/b3/b305375j/

DOI: 10.1039/b305375j

Table 1 Reaction of L-(−)-menthol with the Hendrickson reagent and nucleophiles

Entry[a,b]	Solvent	Nucleophile	Products	Product ratios[c]
1	DCM	4-Nitrobenzoic acid	**5a + 5b** : menthol : **6**	97 : 1 : 2
2	THF	4-Nitrobenzoic acid	**5a + 5b** : menthol : **6**	84 : 12 : 4
3	Toluene	4-Nitrobenzoic acid	**5a + 5b** : menthol : **6**	68 : 10 : 22
4	Toluene[d]	4-Nitrobenzoic acid	**5a + 5b** : menthol : **6**	52 : 48 : 0
5	Toluene	4-Nitrobenzoic acid[e]	**5a + 5b** : menthol : **6**[f]	27 : 0 : 72[f]
6	DCM	4-Nitrobenzoic acid[e]	**5a + 5b** : menthol : **6**	86 : 1 : 13
7	Toluene	Thiol acetic acid	**5a + 5b** : menthol : **7**	38 : 24 : 38
8	DCM	Thiol acetic acid	**5a + 5b** : menthol : **7**	70 : 20 : 10
9	Toluene	4-Methoxybenzoic acid	**5a + 5b** : menthol : **8**	54 : 35 : 11
10	DCM–DMF (2 : 1)	Sodium azide	**5a + 5b** : menthol : **9**	20 : 54 : 26
11	Toluene	$Zn(N_3)_2 \cdot 2Py$	**5a + 5b** : menthol : **9**	92 : 2 : 6

[a] All reactions were carried out with **1** (1.0 eq.), l-(−)-menthol (1.0 eq.), nucleophile (1.0 eq.) and diisopropylethylamine (2.2 eq.) in 10 mL solvent. [b] Reaction conditions were 40 °C for 24 h. [c] Product ratios determined by GC/MS analysis. [d] 100 mL solvent. [e] 4-Nitrobenzoic acid (4.5 eq.) and diisopropylethylamine (5.5 eq.). [f] Ester displays retention and inversion of configuration in the ratio of 88 : 12 by ^{1}H NMR.



(1)

with **1** results in the formation of dienes.[14] There is no known analogy for this using the Mitsunobu reagents. In this paper, we compare and contrast the Hendrickson and Mitsunobu protocols, particularly in relation to the esterification of menthol with 4-nitrobenzoic acid.

Results and discussion

Initially, we examined the use of **1** for the simple esterification of a primary alcohol. The reagent **1** was generated by addition of triflic anhydride to an ice-cold solution of triphenylphosphine oxide in dry dichloromethane (DCM). 4-Nitrobenzyl alcohol, 4-nitrobenzoic acid and diisopropylethylamine were added and after stirring for 2 h at room temperature, work up and chromatography, 4-nitrobenzyl 4-nitrobenzoate **2** was obtained in high (95%) yield. A small excess of the triphenylphosphine oxide was employed to ensure that all of the triflic anhydride was consumed. Excess triflic anhydride could react with the alcohol to form the triflate ester or the carboxylic acid to form the corresponding anhydride. It was important to distil the triflic anhydride from a small amount of P_2O_5 prior to use; without distillation, conversion to ester **2** was 86%; with distillation, conversion to ester **2** was 97.5% by ^{1}H NMR. It was also important to use only 1 equivalent of **1**. Excess **1** led to reduced yields of ester **2** (Fig. 1). The reason for this is not clear, however it may be due to the excess reagent generating a more polar reaction environment thereby slowing the reaction (*cf.* later).

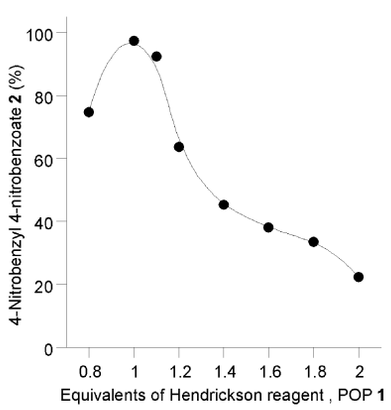


Fig. 1 The effect of equivalents of Hendrickson reagent, **1**, on yield (by ^{1}H NMR) of 4-nitrobenzyl 4-nitrobenzoate **2**. Reagents and conditions: **1** (0.8–2.0 eq.), 4-nitrobenzyl alcohol (1.0 eq., 3 mmol), 4-nitrobenzoic acid (1.0 eq., 3 mmol), diisopropylethylamine (5.3–13.2 eq.) and DCM (10 mL); 2 h at room temperature.

Several other nucleophiles were also investigated briefly. Thus, treatment of **1** with 4-chlorobenzyl alcohol, thiolacetic acid, and diisopropylethylamine in DCM at room temperature overnight gave a 97% yield of 4-chlorobenzyl thioacetate **3**. Similarly, treatment of **1** with 4-chlorobenzyl alcohol, sodium azide, and diisopropylethylamine in 3 : 1 DCM–dimethylformamide (DMF) gave a 93% yield of 4-chlorobenzyl azide **4**. Interestingly, treatment of 4-chlorobenzyl alcohol under Mitsunobu conditions with sodium azide in 3 : 1 DCM–DMF at room temperature overnight gave no reaction, the alcohol being recovered unchanged. It is clear from these examples and the work of Hendrickson[5] that the reagent **1** provides a mild, useful procedure for the esterification of primary alcohols and the synthesis of primary azides.

Esterification of secondary alcohols on the other hand was surprisingly sluggish and resulted in very low yields. Menthol, which has been used previously to investigate the stereochemistry of esterification under Mitsunobu conditions,[15,16] was chosen for this study. Treatment of **1** with the more hindered secondary alcohol (−)-menthol, 4-nitrobenzoic acid and diisopropylethylamine in DCM at room temperature overnight gave no detectable ester formation. The reaction was repeated at 40 °C for 24 h, then quenched and analysed by GC-MS. It was found that the major products formed were the products of elimination, 2- and 3-menthenes **5a** and **5b** (97%), along with small amounts of menthol (1%), and the inverted ester, neomenthyl 4-nitrobenzoate **6** (2%). The reaction was examined under a range of conditions, and with different solvents and different nucleophiles but in almost all cases, the major reaction observed was elimination (Table 1). Comparing entries 1, 2 and 3, toluene was found to give a higher relative yield of inverted ester **6** (and less elimination) than tetrahydrofuran (THF) and DCM, but even here the yield of inverted ester **6** was only 22%. From Table 1, the ratio of elimination to substitution is clearly both solvent dependent and concentration dependent.

Use of an excess of 4-nitrobenzoic acid when DCM was employed (entry 6), did not improve the yield of inverted ester. Use of 4-methoxybenzoic acid instead of 4-nitrobenzoic acid led to a decrease in the yield of inverted ester **8** relative to elimination (entry 9). The only reaction where esterification was the major reaction was when a large excess of 4-nitrobenzoic acid was employed (entry 5). Under these conditions however, the ester formed, menthyl 4-nitrobenzoate,[17] was mainly the product of retention not inversion. Presumably with excess acid, carboxyl group activation or anhydride formation become kinetically competitive leading to menthol acylation with retention. Both the Hendrickson[5] and Mitsunobu[18] reagents are

known to convert carboxylic acids into their corresponding anhydrides.

Use of the much more nucleophilic thiolacetic acid instead of 4-nitrobenzoic acid led to an increase in the ratio of S_N2 substitution product **7** to elimination (entries 7 and 8), but elimination was still a significant pathway. Once again, the least polar solvent toluene gave the highest proportion of S_N2 substitution product **7** (38%). In contrast to the primary alcohol case, treatment of **1** with menthol, sodium azide, and diisopropylethylamine in 2 : 1 DCM–DMF at room temperature overnight gave only a low relative yield (26%) of the expected neomenthyl azide **9** (entry 10).

Use of toluene and the much more soluble zinc azide/pyridine complex at 40 °C for 24 h gave a higher overall conversion but a lower yield (6%) of the azide **9**, the major pathway (92%) being elimination (entry 11). Interestingly Maeda and Ohmori,[19] who generated analogous alkoxytriphenylphosphonium ions of secondary alcohols such as α-cholestanol by an electrochemical procedure, found that these did not undergo S_N2 displacement by azide (Bu_4NN_3) in DCM but did undergo S_N2 displacement by bromide and chloride ions.

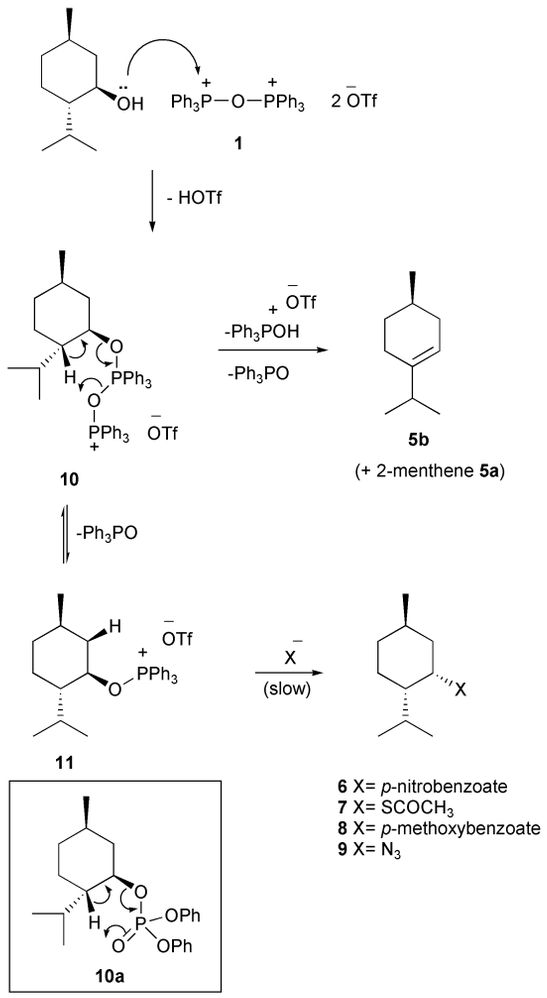
It is clear that with menthol, use of the reagent **1** leads predominantly to elimination, irrespective of the nucleophilic species present. Interestingly, the elimination mechanism cannot be *anti* (E2), as both 2-menthene **5a** and 3-menthene **5b** were formed (ratio ~ 1 : 2, respectively). Hendrickson and Schwartzman[20] have previously reported that **1** reacts with menthol in the presence of potassium carbonate to produce a mixture of menthenes and suggested[5] that *cis* elimination may be favoured. An E1 mechanism would also be consistent with the formation of a mixture of 2- and 3-menthenes **5a** and **5b**. However, this seems less feasible since an intermediate carbocation should be trapped by strong nucleophiles such as azide and thioacetate to give a mixture of menthyl and neomenthyl products, and this was not observed. It is also interesting to note that a similar ratio (1 : 2) of 2- and 3-menthenes **5a**–**5b** was formed by thermolysis of menthyldiphenyl phosphate.[21]

A mechanism for the *cis* elimination is suggested in Scheme 2, by analogy with that for the thermolysis of menthyldiphenyl phosphate (**10a**, mechanism shown for formation of 3-menthene **5b**).

Reaction of menthol with **1** would be expected to result in the initial formation of the mixed phosphorane/phosphonium salt **10**. This could undergo an electrocyclic fragmentation to give the two possible products of *cis* elimination (2- and 3-menthene **5a**–**5b**), or it could eliminate triphenylphosphine oxide to give the normal Mitsunobu intermediate **11**, which could undergo S_N2 displacement by a nucleophile X^- to give the neomenthyl products **6**–**9**. Presumably the latter process is kinetically slow relative to elimination. We were unable to find any ^{31}P NMR evidence for the presence of **10**. Upon mixing menthol with **1** at room temperature, the oxyphosphonium salt **11** is formed immediately as evidenced by both ^{31}P (δ 59.5 ppm) and ^{1}H NMR data (δ 4.25 ppm, dddd which collapsed to a ddd upon phosphorus decoupling).

We also examined a less hindered secondary alcohol. Treatment of cyclohexanol with **1**, 4-nitrobenzoic acid and diisopropylethylamine in DCM at 40 °C for 24 h (same conditions as entry 1, Table 1) gave cyclohexene (66%) as the major product, cyclohexyl 4-nitrobenzoate **12** (28%) and cyclohexanol (6%). It is clear from the contrasting results between primary and secondary alcohols, that steric factors are very important for Hendrickson reagent-mediated esterification and that the greater the degree of steric crowding, the greater the amount of competing elimination. The question is *why* hasn't elimination been observed previously with the Mitsunobu reaction of menthol and 4-nitrobenzoic acid, a well studied reaction[15] described in "*Organic Syntheses*"?[16]

Previous work from this laboratory[10] had shown that the rate of Mitsunobu esterification is markedly dependant on the solvent polarity [for example, the rate of formation of ethyl



Scheme 2

benzoate at 0 °C is approximately 100 times slower in acetonitrile (MeCN) than in THF]. We considered that the presence of salts (diisopropylethylammonium triflate) in reactions involving the Hendrickson reagent would result in a more polar reaction environment, and that this effective increase in solvent polarity might be tipping the balance in favour of elimination over substitution. In order to test this hypothesis, we examined the Mitsunobu esterification of menthol with 4-nitrobenzoic acid in the presence of diisopropylethylammonium triflate by ^{31}P NMR and GC/MS. Initially, several control esterification reactions were carried out in the absence of added salt.

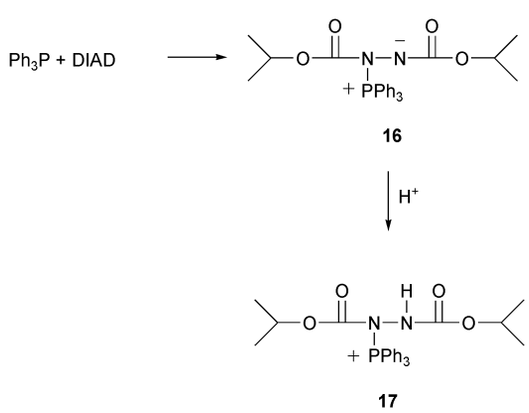
1 Organic syntheses conditions[16]

Under these conditions (menthol, 4-nitrobenzoic acid, TPP, DIAD, THF, rt, 24 h) GC/MS showed the formation of neomenthyl 4-nitrobenzoate **6** (88%) and 2-menthene **5a** (12%). The ester **6** was isolated in 82% yield after chromatography (lit.[16] yield, 85%). It is interesting to note that although alkene formation has previously been observed in the Mitsunobu reaction during the total synthesis of doliculide[22] and with sterically hindered alcohols such as homopropargylic alcohol **13**,[23] cyanoalcohol **14**[24] and lactone **15**,[25] formation of menthene from menthol under Mitsunobu conditions has not been reported previously. Presumably being quite volatile, it is lost during normal work-up and solvent evaporation.

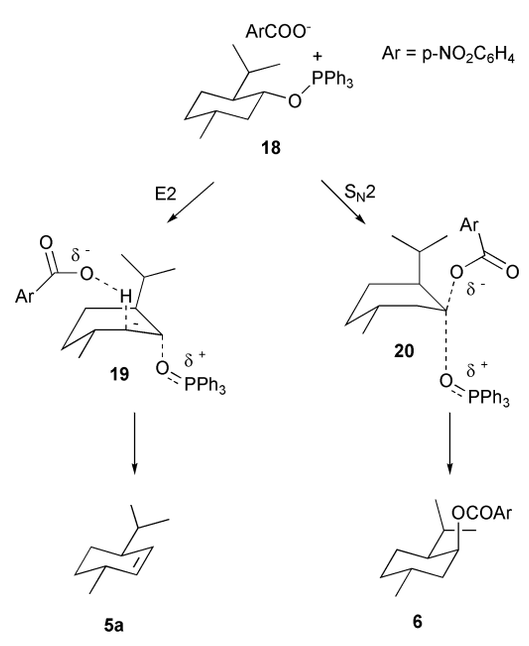
2 Reaction in DCM (preferred solvent for reactions employing the Hendrickson reagent[5] and solvent used for Mitsunobu reactions in the presence of salts)

When the reaction was carried out in CD_2Cl_2 in an NMR tube, the ^{31}P NMR spectrum showed two main signals (ratio ~ 9 : 1)

corresponding[26] to triphenylphosphine oxide (δ 29.1 ppm) and the oxyphosphonium salt **18** (δ 59.5 ppm) (Scheme 4). Analysis by GC/MS gave a yield of neomenthyl 4-nitrobenzoate **6** of approximately 76% along with small amounts of menthol (10%) and 2-menthene **5a** (14%). The reaction was repeated but in the presence of diisopropylethylammonium triflate. This time, the ^{31}P NMR spectrum showed slow formation of the oxyphosphonium salt **18** (δ 59.5 ppm) from the protonated betaine **17** (δ 52.6 ppm) (Scheme 3).[26] After 24 h at room temperature, the ratio of **17** : **18** was approximately 4 : 1. There was very little increase (<5%) in the triphenylphosphine oxide peak over this time indicating that the presence of diisopropylethylammonium triflate was effectively blocking the Mitsunobu reaction. This was presumably due to protonation of the betaine by the diisopropylethylammonium ion, leaving no base to form the alkoxide anion, which, as noted by Hughes *et al.*,[27] is required for oxyphosphonium salt formation. This was confirmed by carrying out the reaction in the presence of an extra 2 equivalents of diisopropylethylamine, which resulted in an increase in the proportion of oxyphosphonium salt **18** (ratio **17** : **18** = 7 : 8). The presence of proton sources however, is also known[27] to slow the S_N2 step of the Mitsunobu reaction through hydrogen bonding with the carboxylate anion, hence the lack of progression of the reaction beyond the oxyphosphonium intermediate stage. In order to avoid the complications of protonation and hydrogen bonding effects, the diisopropylethylammonium triflate was replaced by tetrabutylammonium triflate (n-Bu_4NOTf).



Scheme 3



Scheme 4

A solution of TPP, (−)-menthol and 4-nitrobenzoic acid was prepared in dry DCM and n-Bu_4NOTf in DCM was added followed by the slow addition of DIAD to the reaction mixture cooled in ice. After 24 h at room temperature, the reaction mixture was analysed by GC/MS. The results, showing the effect of the concentration of n-Bu_4NOTf on the outcome of the Mitsunobu reaction, are summarized in Fig. 2. It can be seen that in the presence of one molar equivalent of n-Bu_4NOTf (relative to TPP/DIAD), the normal Mitsunobu esterification reaction is slowed dramatically (4% yield of ester **6**, 18% yield of 2-menthene **5a**, 78% recovered menthol) and elimination has become the major reaction pathway (Fig. 2(a)). These results are in sharp contrast to the results of Walker and coworkers[28] who found that addition of sodium benzoate dramatically accelerated the formation of trifluoroacetate esters. However, as noted by Hughes,[27] a catalytic amount of dissolved benzoate can act as a base and increase the rate of the alcohol activation step. This is not possible in the present case as n-Bu_4NOTf is not basic. Interestingly, the reaction is sensitive to even trace amounts of n-Bu_4NOTf salt (Fig. 2(b)). Thus, in going from no salt to just 0.01 molar equivalents of salt (0.036 mmol salt, 3.6 mmol TPP/DIAD), the ratio of elimination to substitution changed from 0.2 to 1.4. At higher proportions of salt, the ratio of elimination to substitution increased steadily reached 10.4 at 2 molar equivalents of n-Bu_4NOTf. At this level of salt, >80% of the menthol was recovered unreacted after 24 h at room temperature.

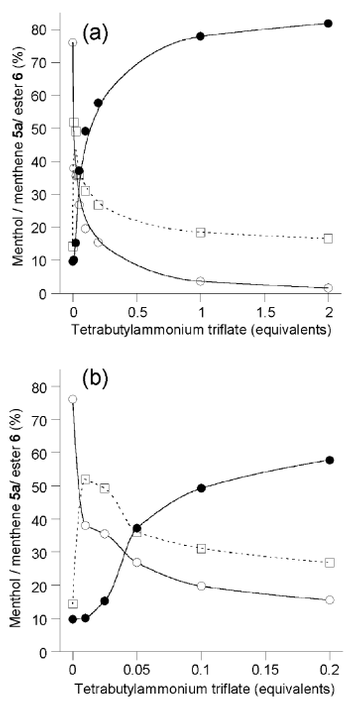


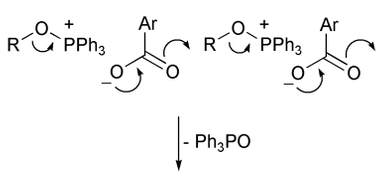
Fig. 2 The effect of added tetrabutylammonium triflate on the outcome of the Mitsunobu reaction between L-(−)-menthol and 4-nitrobenzoic acid. 2-Menthene **5a** (□), L-(–)-menthol (●), (1S,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl-4-nitrobenzoate **6** (○). Reagents and conditions: TPP (1.0 eq.), DIAD (1.0 eq.), L-(–)-menthol (0.85 eq.), 4-nitrobenzoic acid (0.85 eq.), n-Bu_4NOTf (0.0–2.0 eq., Fig. 2(a); 0.0–0.2 eq., Fig. 2(b)) and DCM (8 mL); 24 h at room temperature.

It is clear from these results that salts have a dramatic effect both on the rate of Mitsunobu esterification and on the outcome. Just traces of salts lead to elimination becoming the major reaction pathway rather than S_N2 substitution. Previous work by Hughes[27] has shown that the S_N2 substitution rate is decreased 10-fold by addition of a large amount of a swamping salt (0.5 M Bu_4NBF_4), while previous work from this laboratory[10] has shown that the rate of Mitsunobu esterification is very much slower in polar solvents. Both of these effects are

readily understood in terms of a late transition state (TS) for the S_N2 substitution reaction, a reaction in which the reactants are oppositely charged and the products are neutral (Scheme 4). The formation of such a TS would be favoured by a non-polar reaction environment in accordance with the Hughes–Ingold rules.[29] By the Hammond Postulate[30] the TS would resemble the products.

It is interesting to note that increasing the concentration of n-Bu_4NOTf causes a decrease in both the rate of formation of ester (S_N2 product) and in the rate of formation of 2-menthene **5a** (E2 product), but the effect on the S_N2 process is greater than on the E2 process. This suggests the TS for the E2 process **19** is earlier (less product like) than for the corresponding S_N2 process **20**. With a late TS, steric factors would be expected to be more important, so it is perhaps not surprising that in the case of menthol where the S_N2 transition state **20** is quite crowded that small changes in the reaction environment might tip the balance in favour of the elimination pathway. While the trends can be rationalised in terms of a later TS for the S_N2 process than the E2 process, it is still difficult to explain why *traces* of n-Bu_4NOTf cause such a dramatic turnaround in reaction pathway from substitution to elimination.

One possible explanation is that the mechanism of the Mistunobu esterification reaction involves the formation of ion pair aggregates.[7,28,31–33] In the normal S_N2 process, the alkoxyphosphonium and carboxylate ions must be separated in order to form the S_N2 TS **20** required for backside attack. As noted by Jones *et al.*,[32b] such charge separation can be avoided by ion pair clustering wherein a positive phosphorus ion in one ion pair is in part electrically neutralised by the negative carboxylate moiety in another ion pair (as illustrated in Scheme 5). Traces of salts (or polar solvents) could easily interfere with the formation of such ion pair clusters, thereby inhibiting the S_N2 process. The corresponding E2 process (**19**) could be brought about by any Lewis base present in the reaction medium, not just the carboxylate ion shown. Thus, ion pair clustering is not necessary for the E2 elimination process.



Scheme 5

One other factor that affects the rate and overall outcome of the Mitsunobu reaction is that whereas the oxyphosphonium ion intermediate **11**, is formed immediately upon mixing menthol and **1** at room temperature, reaction of menthol with the Mitsunobu reagents to give the same oxyphosphonium ion **11** (or **18**) occurs much more slowly. Thus, a mixture of menthol, 4-nitrobenzoic acid, and n-Bu_4NOTf was treated with a slight excess of DIAD and TPP in cold, dry CD_2Cl_2 under nitrogen. The ^{31}P NMR spectrum showed 3 major peaks, corresponding to the oxyphosphonium salt **11** (δ 59.5 ppm, 22%), the betaine **16** (δ 44.2 ppm,[34] 58%)) and triphenylphosphine oxide (δ 29.1 ppm, 20%). After 24 h at room temperature, triphenylphosphine oxide had become the major peak (71%) presumably due to competing acylation of the hydrazine.[17,35] The oxyphosphonium salt **11** was still present (16%) and there was a small amount of protonated betaine **17** (13%). The much faster rate of reaction of menthol with **1** is not surprising as the phosphonium center in **1** would be expected to be more electrophilic than the phosphonium center in **16** or **17**, and triphenylphosphine oxide is a much better leaving group than the hydrazide anion. Thus, the oxyphosphonium ion is being generated, but in the presence of n-Bu_4NOTf, it is relatively stable, undergoing slow elimination to give 2-menthene **5a**, and a minor amount of S_N2 displacement to form neomenthyl 4-nitrobenzoate **6**. When both the E2 and S_N2 processes are sufficiently slow, side reactions such as acylation of the hydrazine can become competitive,[17,35] so that most of the menthol is recovered at the end of the reaction (Fig. 2(a)).

One other intriguing difference between the Mitsunobu- and Hendrickson-induced elimination reactions with menthol is that the Mistunobu reaction resulted in stereospecific *anti* elimination to give only 2-menthene (**5a**), whereas the Hendrickson reagent resulted in the formation of 3-menthene (**5b**) as the major product (ratio 3-menthene **5b** : 2-menthene **5a** = 2 : 1). It is difficult to reconcile such differences if both the Hendrickson and Mitsunobu reactions take place *via* a common intermediate (**18**). However, if the Hendrickson reagent results in the initial formation of intermediate **10**, then *cis* elimination becomes feasible (Scheme 2). We thought that it might be possible to convert the Mitsunobu intermediate **18** into an intermediate analogous to **10** by carrying out a Mitsunobu reaction in the presence of a large excess of triphenylphosphine oxide. However, even in the presence of a 5-fold excess of triphenylphosphine oxide (relative to TPP, DIAD and menthol – no 4-nitrobenzoic acid was added in this experiment) only 2-menthene **5a** was formed.

Conclusion

^{31}P NMR evidence suggests that both the Hendrickson reagent and Mitsunobu reagent generate the same menthyloxyphosphonium ion intermediate, but the reaction outcome is different in each case. The major reaction pathway under Mitsunobu conditions is inverted ester formation (86%) with only a minor amount (14%) of competing elimination. Elimination is *anti* to give exclusively 2-menthene **5a**. When the Hendrickson reagent is used, however, the major reaction pathway is elimination (97%), and elimination appears to be *syn*, to give a 2 : 1 mixture of 3- and 2-menthenes **5a : 5b**, respectively. The ratio of esterification to elimination can be increased significantly by employing a non-polar solvent (toluene instead of DCM).

The difference between the two reactions appears to be related to the more 'ionic' conditions generated when the Hendrickson reagent is employed. When the Mitsunobu esterification reaction of menthol is carried out under analogous 'ionic' conditions (in the presence of salts), elimination also becomes the dominant reaction pathway. With primary alcohols, substitution is the dominant pathway with both the Hendrickson and Mitsunobu reagents. As a general rule, **1** can be used as an alternative to the Mitsunobu reaction for replacement of a primary hydroxyl by various nucleophiles. With some nucleophiles (such as sodium azide) the more 'ionic' nature of **1** brings about reactions where the Mitsunobu reaction fails.

Experimental

General methods

All reactions were carried out in flame-dried glassware under an inert atmosphere. THF was freshly distilled from sodium benzophenone ketal, toluene from sodium and DCM from calcium hydride. Triflic anhydride was distilled from a small amount of phosphorus pentoxide before use. Diisopropylethylamine was distilled from potassium hydroxide and stored over molecular sieves. All other reagents were purchased from commercial suppliers and used without further purification. Flash chromatography was carried out using a Biotage system with pre-packed silica columns. Melting points were determined by the capillary method and are uncorrected. IR spectra were recorded on a Thermo Nicolet-Nexus FTIR apparatus. Elemental analyses

were performed at the University of Queensland. ^{1}H NMR spectra were obtained at either 200 or 400 MHz and chemical shifts are reported in parts per million, using the appropriate signal for solvent protons as a reference. ^{13}C NMR spectra were recorded at 100 MHz and ^{31}P NMR spectra at 162 MHz with an internal reference of phosphoric acid (H_3PO_4). GC/MS analyses were performed on a gas chromatograph (20 m db-5 ms capillary column) equipped with a mass-selective detector. The identity of products was confirmed by ^{1}H NMR, which agreed with those reported in the literature, and by means of co-injection of authentic samples.

The mixture of 2- and 3-menthenes **5a**–**b** was prepared by thermolysis of the diphenylphosphate ester of menthol.[21] Authentic samples of (1*S*,2*S*,5*R*)-5-methyl-2-(1-methylethyl)-cyclohexyl-4-nitrobenzoate **6**,[16] (+)-neomenthyl thioacetate **7**,[36] (1*S*,2*S*,5*R*)-5-methyl-2-(1-methylethyl)cyclohexyl-4-methoxy-benzoate **8**,[15] (1*S*,2*S*,5*R*)-5-methyl-2-(1-methylethyl)cyclohexyl-azide **9**[37] and cyclohexyl 4-nitrobenzoate **12** (mp 49–51 °C, lit.,[38] 47–48 °C) were generated by standard Mitsunobu protocols. The zinc azide/bis-pyridine complex was prepared from zinc nitrate and sodium azide.[37]

Typical example for the synthesis of 4-nitrobenzyl 4-nitrobenzoate 2 using 1.0 equivalent of Hendrickson reagent, 1

Addition of triflic anhydride (0.5 mL, 3 mmol) to an ice-cooled solution of triphenylphosphine oxide (2 g, 7.2 mmol) in dry DCM (10 mL) generated a white precipiate which was stirred at 0 °C for 30 min. 4-Nitrobenzyl alcohol (0.46 g, 3 mmol), 4-nitrobenzoic acid (0.5 g, 3 mmol) and diisopropylethylamine (1.15 mL, 6.6 mmol) were added in succession to form a yellow solution. After stirring for 2 h at room temperature, the mixture was washed with saturated aqueous $NaHCO_3$ and water. The organic layers were combined, dried ($MgSO_4$) and concentrated *in vacuo*. Analysis by ^{1}H NMR revealed 97.5% conversion of the benzyl alcohol to 4-nitrobenzyl 4-nitrobenzoate **2**. Purification by flash chromatography (eluent DCM–hexane, 1 : 1) afforded 4-nitrobenzyl 4-nitrobenzoate **2** as a yellow solid (0.86 g, 95%). Mp 165–167 °C (lit.,[39] 168 °C).

Synthesis of 4-chlorobenzyl thioacetate 3 using 1 and thiolacetic acid

Triflic anhydride (0.34 mL, 2 mmol) was added to triphenylphosphine oxide (1.34 g, 4.8 mmol) in dry DCM (10 mL) as above. 4-Chlorobenzyl alcohol (0.29 g, 2 mmol), thiol acetic acid (0.143 mL, 2 mmol) and diisopropylethylamine (0.77 mL, 4.4 mmol) were added to generate a homogeneous solution that was allowed to warm to room temperature overnight. The resulting mixture was washed with aqueous saturated $NaHCO_3$ (2 × 20 mL) and water (2 × 20 mL) and dried ($MgSO_4$). The organic layers were combined and reduced *in vacuo* to afford a yellow residue that was purified by flash chromatography, using DCM–hexane (1 : 1) as eluent. 4-Chlorobenzyl thioacetate **3** was obtained as a yellow oil (0.39 g, 97%) (Found: C, 53.62; H, 4.53. Calc. for C_9H_9ClOS: C, 53.86; H, 4.52%); ν_{max} (Nujol)/cm^{-1} 1703, 1133, 1094; δ_H (400 MHz, $CDCl_3$) 2.36 (s, 3H), 4.08 (s, 2H), 7.17 (d, J = 8.7 Hz, 2H), 7.27 (d, J = 8.7 Hz, 2H); δ_C (100 MHz, $CDCl_3$) 30.3, 32.7, 128.7, 130.1, 133.0, 136.2, 194.8; (ESMS +) *m*/*z* 199 (^{35}Cl MH$^+$, 10%), 201 (^{37}Cl MH$^+$, 3%).

Synthesis of 4-chlorobenzyl azide 4 using 1 and NaN_3

Treatment of an ice-cooled solution of triphenylphosphine oxide (1.34 g, 4.8 mmol) in DCM (10 mL) with triflic anhydride (0.34 mL, 2 mmol) generated a white precipitate which was stirred at 0 °C for 30 min. 4-Chlorobenzyl alcohol (0.29 g, 2 mmol), a solution of sodium azide (0.2 g, 3 mmol) in DMF (3 mL) and diisopropylethylamine (0.77 mL, 4.4 mmol) were added consecutively and the solution left to warm to room temperature overnight. The cloudy yellow mixture was washed with aqueous saturated $NaHCO_3$ (2 × 20 mL) and water (2 × 20 mL), then dried ($MgSO_4$). The combined organic layers were concentrated *in vacuo* and the resulting residue submitted to flash chromatography to remove the phosphine oxide. Elution with DCM–hexane (1 : 1) afforded 4-chlorobenzyl azide **4** as a colourless oil (0.31 g, 93%); n_D ^{15}1.5556 (lit.,[40] 1.5600); ν_{max} (Nujol)/cm^{-1} 2100; δ_H (400 MHz, $CDCl_3$) 4.33 (s, 2H), 7.26 (d, J = 8.5 Hz, 2H), 7.37 (d, J = 8.5 Hz, 2H); δ_C (100 MHz, $CDCl_3$) 54, 129, 129.5, 133.9, 134.2; HRMS (Found: *m*/*z* 167.02495. $C_7H_6ClN_3$ requires 167.02502).

Attempted synthesis of 4-chlorobenzyl azide using triphenylphosphine, DIAD and NaN_3

To a solution of TPP (1 g, 3.81 mmol) and 4-chlorobenzyl alcohol (0.46 g, 3.2 mmol) in DCM (10 mL) was added sodium azide (0.27 g, 4 mmol) in DMF (4 mL). The heterogenous mixture was cooled on ice and DIAD (0.75 mL, 3.81 mmol) added slowly. After 30 min, the solution was left to warm to room temperature overnight. The reaction mixture was washed with aqueous saturated $NaHCO_3$ (2 × 25 mL) and water (2 × 25 mL), then dried ($MgSO_4$). Concentration of the organic layers *in vacuo* yielded a pale yellow residue that was shown to contain unreacted 4-chlorobenzyl alcohol by ^{1}H NMR analysis.

Representative example for the reaction of the Hendrickson reagent with a secondary alcohol and nucleophile: attempted synthesis of (1*S*,2*S*,5*R*)-5-methyl-2-(1-methylethyl)cyclohexyl-4-nitrobenzoate 6

Triflic anhydride (0.5 mL, 3 mmol) was added slowly to an ice-cooled solution of triphenylphosphine oxide (2 g, 7.2 mmol) in dry DCM (10 mL). A white solid precipitated immediately and the solution was stirred at 0 °C for 30 min. The DCM was removed *in vacuo* and the remaining solid re-suspended in dry toluene (10 mL). Addition of (1*R*,2*S*,5*R*)-(−)-menthol (0.46 g, 3 mmol) to the slurry generated a clear solution over 5 min, to which the remaining 4-nitrobenzoic acid (0.5 g, 3 mmol) and diisopropylethylamine (1.15 mL, 6.6 mmol) were added. The resulting yellow solution was warmed at 40 °C for 24 h. The reaction mixture was then quenched using aqueous saturated $NaHCO_3$ and an aliquot of the organic phase analysed directly by GC/MS. The identity of the products generated was confirmed by ^{1}H NMR.

NMR study of (−)-menthoxytriphenylphosphonium triflate 11 formation

A solution of triphenylphosphine oxide (0.1 g, 0.36 mmol) was dissolved in dry CD_2Cl_2 (0.75 mL) in a 5 mm NMR tube. The tube was cooled on ice and triflic anhydride (29 μL, 0.17 mmol) added. A white solid formed immediately and after 10 min, (1*R*,2*S*,5*R*)-(−)-menthol (0.027 g, 0.17 mmol) was added. Brief mixing (vortex) generated a clear solution which showed (by ^{1}H NMR) complete conversion of (−)-menthol to (−)-menthoxytriphenylphosphonium triflate **11**. The ^{31}P NMR spectrum revealed a 1 : 1 mixture of (−)-menthoxytriphenylphosphonium triflate **11** and protonated triphenylphosphine oxide. δ_P (162 MHz, CD_2Cl_2) 51.4 (br s); 59.5 (s). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 4.25 (dddd, J = 10.7, 10.7, 6.6, 4.6 Hz, 1H, H3). The key ^{31}P and ^{1}H NMR peaks for (−)-menthoxytriphenylphosphonium triflate **11** were in agreement with the literature.[19,33]

Formation of 2-menthene 5a and neomenthyl 4-nitrobenzoate 6 (organic syntheses Mitsunobu procedure)[16]

A solution of TPP (4.02 g, 15.32 mmol), (1*R*,2*S*,5*R*)-(−)-menthol (0.6 g, 3.84 mmol) and 4-nitrobenzoic acid (2.58 g, 15.44 mmol) in dry THF (30 mL) was cooled on ice. DIAD (3.03 mL, 15.4 mmol) was added slowly and the reaction left to warm to room temperature overnight. A sample of the reaction

mixture was removed for GC/MS analysis which showed menthene **5a**:neomenthyl 4-nitrobenzoate **6** = 12 : 88. The remaining solution was diluted with ether (30 mL) and washed with saturated aqueous sodium bicarbonate (2 × 20 mL). The aqueous layers were combined and extracted with ether (20 mL). The combined etheral layers were dried ($MgSO_4$) and concentrated *in vacuo*. The resulting solid was suspended in ether (10 mL) and allowed to stand overnight. Hexane (5 mL) was added slowly to the stirring mixture and the precipitated white solid removed by filtration. The solvent was removed from the filtrate and the resulting residue submitted to column chromatography (8% ether–hexanes as eluent) to yield (1*S*,2*S*,5*R*)-5-methyl-2-(1-methylethyl)cyclohexyl-4-nitrobenzoate **6** as a pale yellow crystalline solid (0.96 g, 82%). Mp 92–94 °C, (lit.,[16] 93–95 °C).

^{31}P NMR study of oxyphosphonium salt formation in the presence of $Pr^i_2NH^+EtOTf^-$

A solution of triflic acid (28 μL, 0.32 mmol) and diisopropylethylamine (56 μL, 0.32 mmol) in CD_2Cl_2 (0.75 mL) was prepared in a 5 mm NMR tube. TPP (100 mg, 0.38 mmol), (1*R*,2*S*,5*R*)-(−)-menthol (50 mg, 0.32 mmol) and 4-nitrobenzoic acid (55 mg, 0.32 mmol) were added. A chilled solution of DIAD (75 μL, 0.38 mmol) was then added to the tube at 0 °C. The tube was stoppered and sealed with parafilm. After brief mixing by vortex, a ^{31}P NMR spectrum was obtained at 25 °C and again after standing at room temperature 24 h. The above procedure was repeated using an excess of diisopropylethylamine (168 μL, 0.96 mmol) and in the absence of $Pr^i_2NH^+EtOTf^-$.

At 25 °C: δ_P (162 MHz, CD_2Cl_2) 29.1 (s), 52.6 (s), 2 : 3, respectively; at 25 °C after 24 h: δ_P 29.1 (s), 52.6 (s), 59.5 (s), 47 : 42 : 11, respectively; with an excess of diisopropylethylamine at 25 °C: δ_P 29.1 (s), 52.6 (s), 53 : 47, respectively; with an excess of diisopropylethylamine at 25 °C after 24 h: δ_P 29.1 (s), 52.6 (s), 59.5 (s), 55 : 21 : 33, respectively; in the absence of $Pr^i_2NH^+EtOTf^-$ at 25 °C after 24 h: δ_P 29.1 (s), 59.5 (s), 9 : 1, respectively.

General procedure for the addition of tetrabutylammonium triflate to the standard Mitsunobu reaction

A solution of TPP (1 g, 3.8 mmol), (1R,2S,5R)-(−)-menthol (0.5 g, 3.2 mmol) and 4-nitrobenzoic acid (0.55 g, 3.2 mmol) was prepared in dry DCM (8 mL). Tetrabutylammonium triflate (0.01–2 eq., 0.038–7.6 mmol) in DCM (2 mL) was added. Slow addition of DIAD (0.75 mL, 3.8 mmol) to the ice-cooled liquid generated a yellow solution that was left to warm to room temperature over 24 h. An aliquot of the reaction mixture was removed for GC/MS analysis.

^{31}P NMR study of oxyphosphonium salt formation in the presence of $Bu_4N^+OTf^-$

A solution of TPP (0.1 g, 0.38 mmol) in CD_2Cl_2 (0.75 mL) was prepared in a 5 mm NMR tube. Tetrabutylammonium triflate (0.15 g, 0.38 mmol), (1*R*,2*S*,5*R*)-(−)-menthol (50 mg, 0.32 mmol) and 4-nitrobenzoic acid (55 mg, 0.32 mmol) were added. A chilled solution of DIAD (75 μL, 0.38 mmol) was then added to the tube at 0 °C. The tube was stoppered, sealed with parafilm and briefly vortexed. A ^{31}P NMR spectrum was obtained at 25 °C and again after standing at room temperature 24 h.

At 25 °C: δ_P (162 MHz, CD_2Cl_2) 29.1 (s), 44.2 (s), 59.5(s) ~1:3 : 1, respectively; at 25 °C after 24 h: δ_P 29.1 (s), 52.6 (s), 59.5 (s), ~5 : 1 : 1, respectively.

Addition of excess triphenylphospine oxide to a standard Mitsunobu reaction (in the absence of 4-nitrobenzoic acid)

A solution of TPP (1 g, 3.8 mmol), triphenylphosphine oxide (4.45 g, 16 mmol) and (*1R,2S,5R*)-(−)-menthol (0.5 g, 3.2 mmol) was prepared in dry THF (25 mL). Addition of DIAD (0.75 mL, 3.8 mmol) to the ice-cooled solution generated a yellow solution which was left to warm to room temperature overnight. A sample was then removed for GC/MS analysis and the remaining solution concentrated *in vacuo*. Analysis by both GC/MS and ^{1}H NMR confirmed complete conversion of menthol to 2-menthene **5a**.

Acknowledgements

We gratefully acknowledge financial support for this work from the Australian Research Council and Griffith University and the support of Natural Product Discovery, Griffith University, formerly AZGU.

References

1 O. Mitsunobu, *Synthesis*, 1981, 1–28.
2 D. L. Hughes, *Org. React.*, 1992, **42**, 335–656.
3 I. D. Jenkins and O. Mitsunobu, in *Encyclopaedia of Reagents for Organic Synthesis*, ed. L. A. Paquette, Wiley, 1995, vol. 8, pp. 5379–5390.
4 D. L. Hughes, *Org. Prep. Proced. Int.*, 1996, **28**(2), 127–164.
5 J. B. Hendrickson, *Encyclopaedia of Reagents for Organic Synthesis*, ed. L. A. Paquette, Wiley, 1995, vol. 8, pp. 5405–5407.
6 (*a*) J. B. Hendrickson and Md. S. Hussoin, *J. Org. Chem.*, 1987, **52**, 4137–4139; (*b*) J. B. Hendrickson and Md. S. Hussoin, *J. Org. Chem.*, 1989, **54**, 1144–1149; (*c*) J. B. Hendrickson and Md. S. Hussoin, *Synlett*, 1990, 423–424.
7 S. Ramos and W. Rosen, *Tetrahedron Lett.*, 1981, **22**, 35–38.
8 J. B. Hendrickson, M. Singer and Md. S. Hussoin, *J. Org. Chem.*, 1993, **58**, 6913–6914.
9 (*a*) D. Camp and I. D. Jenkins, *Aust. J. Chem.*, 1988, **41**, 1835–1839; (*b*) M. von Itzstein and M. Mocerino, *Synth. Commun.*, 1990, **20**, 2049–2057; (*c*) M. von Itzstein, M. J. Jenkins and M. Mocerino, *Carbohydr. Res.*, 1990, **208**, 287–288.
10 P. Harvey, PhD thesis, Griffith University, 1996.
11 M. von Itzstein and I. D. Jenkins, *Aust. J. Chem.*, 1983, **36**, 557–563; M. von Itzstein and I. D. Jenkins, *Aust. J. Chem.*, 1983, **37**, 2447–2479.
12 D. Camp and I. D. Jenkins, *Aust. J. Chem.*, 1992, **45**, 47–55.
13 M. von Itzstein and I. D. Jenkins, *J. Chem. Soc., Perkin Trans., 1*, 1986, 437–445; M. von Itzstein and I. D. Jenkins, *J. Chem. Soc., Perkin Trans., 1*, 1987, 2057–2060.
14 J. B. Hendrickson, M. A. Walker, A. Varvak and Md. S. Hussoin, *Synlett*, 1996, 661–662.
15 J. A. Dodge, J. I. Trujillo and M. Presnell, *J. Org. Chem.*, 1994, **59**, 234–236.
16 J. A. Dodge, J. S. Nissen and M. Presnell, *Org. Synth.*, 1996, **73**, 110–115.
17 J. A. Gómez-Vidal, M. T. Forrester and R. B. Silverman, *Org. Lett.*, 2001, **3**, 2477–2479.
18 P. J. Harvey, M. von Itzstein and I. D. Jenkins, *Tetrahedron*, 1997, **53**, 3933–3942.
19 H. Maeda and H. Ohmori, *Acc. Chem. Res.*, 1999, **32**, 72–80.
20 J. B. Hendrickson and S. M. Schwartzman, *Tetrahedron Lett.*, 1975, 277–280.
21 H. Quast and T. Dietz, *Synthesis*, 1995, 1300–1304.
22 H. Ishiwata, H. Sone, H. Kigoshi and K. Yamada, *Tetrahedron*, 1994, **50**, 12853–12882.
23 R. W. Friesen and S. Bissada, *Tetrahedron Lett.*, 1994, **35**, 5615–5618.
24 P. Castejon, A. Moyano, M. A. Pericas and A. Riera, *Tetrahedron*, 1996, **52**, 7063–7086.
25 H. Oikawa, T. Kagawa, T. Kobayashi and A. Ichihara, *Tetrahedron Lett.*, 1996, **37**, 6169–6172.
26 D. Camp and I. D. Jenkins, *J. Org. Chem.*, 1989, **54**, 3045–3049.
27 D. L. Hughes, R. A. Reamer, J. J. Bergan and J. J. Grabowski, *J. Am. Chem. Soc.*, 1988, **110**, 6487–6491.
28 M. Varasi, K. A. M. Walker and M. L. Maddox, *J. Org. Chem.*, 1987, **52**, 4235–4238.
29 C. Reichardt, *Solvent and Solvent Effects in Organic Chemistry*, 2nd edn., 1988, vol. 5, pp. 137—147.
30 G. S. Hammond, *J. Am. Chem. Soc.*, 1955, **77**, 334–338.
31 D. Camp and I. D. Jenkins, *J. Org. Chem.*, 1989, **54**, 3049–3054.
32 (*a*) R. G. Weiss and E. I. Snyder, *J. Org. Chem.*, 1970, **35**, 1627–1632; (*b*) L. A. Jones, C. E. Sumner, Jr., B. Franzus, T-S. Huang and E. I. Snyder, *J. Org. Chem.*, 1978, **43**, 2821–2827; (*c*) J. D. Slagle, T-S. Huang and B. Franzus, *J. Org. Chem.*, 1981, **46**, 3526–3530.

33 S. Ramos and W. Rosen, *J. Org. Chem.*, 1981, **46**, 3530–3533.
34 R. D. Guthrie and I. D. Jenkins, *Aust. J. Chem.*, 1982, **35**, 767–774.
35 D. L. Hughes and R. A. Reamer, *J. Org. Chem.*, 1996, **61**, 2967–2971.
36 B. Strijtveen and R. M. Kellogg, *J. Org. Chem.*, 1986, **51**, 3664–3671.
37 M. C. Viaud and P. Rollin, *Synthesis*, 1990, 130–132.
38 C. J. O'Connor, A. S. H. Mitha and P. Walde, *Aust. J. Chem.*, 1986, **39**, 249–257.
39 E. Lyons and E. E. Reid, *J. Am. Chem. Soc.*, 1917, **39**, 1727–1735.
40 H. Hayashi, A. Ohno and S. Oka, *Bull. Inst. Chem. Res., Kyoto Univ.*, 1975, **53**, 489–493.