Wittig Reactions in Water Media Employing Stabilized Ylides with Aldehydes. Synthesis of α,β-Unsaturated Esters from Mixing Aldehydes, α-Bromoesters, and Ph3P in Aqueous NaHCO3

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Wittig Reactions in Water Media Employing Stabilized Ylides with Aldehydes. Synthesis of α,β-Unsaturated Esters from Mixing Aldehydes, α-Bromoesters, and Ph_3P in Aqueous $NaHCO_3$

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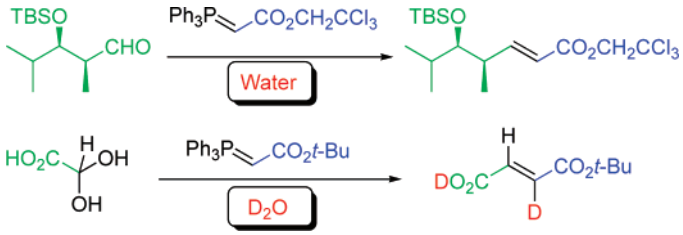

Water is demonstrated to be an effective medium for the Wittig reaction over a wide range of stabilized ylides and aldehydes. Despite sometimes poor solubility of the reactants, good chemical yields normally ranging from 80 to 98% and high *E*-selectivities (up to 99%) are achieved, and the rate of the reactions in water is unexpectedly accelerated. The efficiency of water as a medium in the Wittig reaction is compared to conventional organic solvents ranging from carbon tetrachloride to methanol. The aqueous Wittig reaction works best when large hydrophobic entities are present, such as aromatic, heterocyclic aromatic carboxaldehydes, and long-chain aliphatic aldehydes with triphenylphosphoranes. The *E*/*Z*-isomeric ratio of the Wittig products appears dependent on the electron-accepting/donating capacity and the location of the substituents present in the aromatic ring. The effect of additives, such as benzoic acid, LiCl, and sodium dodecyl sulfate (SDS), on the Wittig reaction has been explored. The Wittig reaction can also be conducted in the presence of acidic entities, such as phenols and carboxylic acids. In addition, large α-substituents in the aliphatic aldehydes do not jeopardize the reaction. It is also demonstrated that hydrates of aldehydes can be used directly in the aqueous Wittig reaction as substrates. The scope of the aqueous Wittig reaction is extended to 24 examples of one-pot mixtures of Ph_3P, α-bromoesters, and aldehydes in sodium bicarbonate solution (at 20 °C for 40 min to 3 h) to provide Wittig products of up to 99% yield and up to 98% *E*-selectivity. Since water is inexpensive, extremely easy to handle, and represents no environmental concerns, it should be considered a possible medium for new organic reactions.

Introduction

A quarter of a century ago, Breslow[1] and Grieco[2] demonstrated that hydrophobic interactions can have a considerable effect on the rate of organic reactions in water. Despite this ground-breaking discovery, however, it was not until recently that the potential of water as a medium in organic reactions has gained widespread focus.[3] It is not entirely surprising that little research has been conducted in this area during the intervening years, given likely concerns over the reactant solubility, impeding catalytic activity, and possible obstruction of functional groups. Nonetheless, significant advances in recent years[3c] have been made toward conducting organic reactions

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in water via the attraction between hydrophobic moieties of the reactants.[4]

In water, there is a strong association between hydrophobic surfaces, and in addition, water excludes nonpolar functional groups reducing the Gibbs energy of solvation. Due to this "hydrophobic effect,"[5] water not only increases the reaction rates but also improves the selectivities of the Diels−Alder [4 + 2] cycloaddition reaction even though the reactants are poorly soluble in water. Considerable experimental and theoretical work has been done to explain the mechanism behind this phenomenon. Several interpretations have been proposed, including the hydrophobic association of the reactants,[1a] micellar catalysis,[1b] solvophobicity,[6] Lewis acid-like catalysis by enhanced hydrogen bonding at the transition state,[7] cohesive energy density,[8] and ground-state destabilization.[9] In a recent paper, Sharpless postulated the possibility of unique properties of the molecules at the macroscopic phase boundary between water and insoluble hydrophobic moieties in order to rationalize the "on water" phenomenon.[4] Besides the Diels−Alder cycloadditions,[10] Claisen rearrangements,[11] ene reactions,[4] Claisen/Diels−Alder cycloaddition,[12] and recently Wittig reactions[13] have been reported to undergo rate increases in spite of the poor solubility of the reactants when conducted in water media.

The Wittig reaction[14] is a very important tool in synthetic organic chemistry since it generates a carbon−carbon double bond normally with a high level of regioselectivity.[15] Despite the long history of the Wittig reaction, it is still under intense mechanistic investigation both by NMR spectroscopy[16] and by computational modeling.[17] The geometrical *Z*-alkene product is preferred for a nonstabilized ylide, while the *E*-alkene is generally the main product when a stabilized ylide is employed. Traditional olefination reaction conditions that provide an excess of the *E*-alkenes include the use of a stabilized ylide and an aldehyde often in solvents ranging from benzene or toluene to DMF or DMSO. It has been recognized that Wittig reactions employing stabilized ylides with aldehydes proceed more slowly, especially in nonpolar solvents.[18]

Various conditions have been reported to improve the Wittig reaction, such as increasing temperature[19] or pressure,[20] using additives,[21] irradiation with microwaves[22] or light,[23] sonication,[24] silica gel,[18] ionic solvents,[25] and recently neat water.[13] A few recent reports that described the influence of aqueous LiCl[26a,b] and a surfactant[27] have also appeared. The efficiency of the aqueous LiCl/LiOH system using PPh_3, α-bromoesters, and aldehydes in Wittig reactions was also reported.[26c] Recent advances also include generation of phosphorus ylides in solid-state reactions by mixing phosphonium salts with anhydrous K_2CO_3 and subsequent Wittig reaction in a solvent-free environment.[28] In the synthesis toward stilbene type products, Aggarwal et al. recently prepared a new class of semistabilized ylides from phosphites, where these ylides displayed very high *E/Z*-selectivity compared to that of the corresponding triphenylphosphonium derivatives conventionally used in Wittig reactions.[29]

Although water has been applied as a medium for Wittig reactions employing elegantly modified water-soluble phosphonium salts,[30,31] the application of water as the essential medium for performing Wittig reactions utilizing poorly water-soluble stabilized ylides is very limited. Herein we present an extension of our initial report[13] pertaining to the Wittig reaction employing hydrophobic triphenylphosphoranes in water as the single reaction medium.[32] Specifically, we examined the relative rates of the Wittig reactions in water compared to those conducted in conventional organic solvents. Furthermore, the influence of additives on the course of the Wittig reaction in water is reported. We also present an extension of our work utilizing the aqueous in situ preparation of ylides and their subsequent

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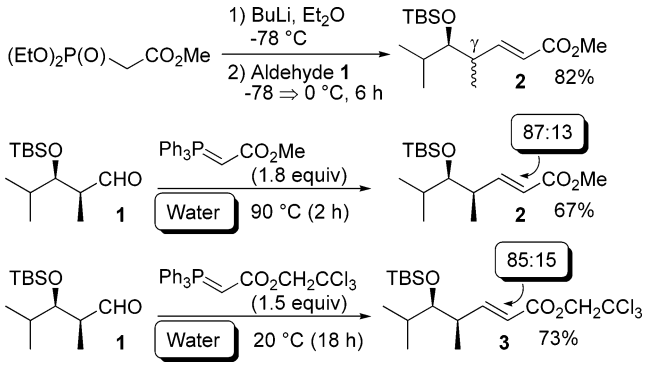
SCHEME 1



Wittig reaction in water. Aside from the application of this work to *greener chemistry*,[33] these results contribute a valuable methodology for carbon−carbon double bond construction in water in synthetic organic chemistry.

Results and Discussion

Water is described as a "medium" rather than a "solvent" in the following context[34] since the reactants appear to be highly insoluble during the course of the aqueous Wittig reactions. Demonstrated herein is the Wittig reaction utilizing stabilized ylides in water as a very efficient medium. Although the starting materials and products appear to be poorly soluble in the medium, the rate of the reaction is unexpectedly fast in water. In a separate project, enoate **2** is an important fragment of one specific target molecule. Conceivably, ester **2** could be obtained from aldehyde **1** and an efficient carbon−carbon double formation reaction. Indeed, compound **2** has previously been synthesized from optically active aldehyde **1** in a Wittig reaction conducted in either refluxing CH_2Cl_2 (70%, 4 weeks!)[35] or refluxing CH_3CN (95%, 18 h).[36] With these data at hand, we examined the corresponding Horner−Wadsworth−Emmons (HWE) reaction utilizing the corresponding phosphonate enolate with aldehyde **1** in an aprotic solvent (Scheme 1). Although this reaction provided a good yield (82%) of intermediate **2**, the reaction was detrimental to the γ-stereocenter which epimerized completely. This result underscores the importance of using less basic olefination reagents such as the corresponding (Wittig) phosphorane in the synthesis of ester **2**.

Inspired by the reports by Breslow,[1] Grieco,[11] and the recent work of Sharpless[4,37] and Nicolaou[12] investigating aqueous organic transformations, we tested the Wittig reaction in water. Even though the substrate (**1**), reagents, and products seem insoluble during the course of the reaction in water, the isolated yield of esters **2** and **3** were good (67−73%) and no epimerization occurred at the γ-stereocenter. These rapidly stirred or shaken reactions could be conducted in capped drum vials (20 mL) either for a shorter time at 90 °C utilizing 1.8 equiv of the phosphorane[38] or for a longer time at 20 °C using 1.5 equiv of the corresponding 2,2,2-trichloroethoxyphosphorane to give ester **3**. The *E/Z*-isomeric ratios seem consistent with one another even though these geometrical isomeric ratios are to some extent lower than the ratios obtained when conducting the Wittig reaction in conventional organic solvents.

Encouraged by the surprising impact of water as a medium in these initial Wittig reactions employing the triphenylphosphoranes, we conducted a broader investigation of this reaction by determining the yields and *E/Z*-ratios utilizing various conventional organic solvents and comparing them to the same reactions conducted in water (Table 1). We intentionally selected two aldehydes that are known to give modest to low *E/Z*-ratios (*o*-anisaldehyde and cinnamaldehyde) upon exposure to stabilized ylides. Methoxycarbonylmethylenetriphenylphosphorane was added to the aldehydes in 5 mL of the medium, and the mixture was then vigorously stirred for either 1 or 2 h at 20 °C. In order to be able to measure the relative rate of the Wittig reaction, the ylide was hydrolyzed using 1.0 M hydrochloric acid to ensure that no Wittig product is formed during the extraction with organic solvent. The *E/Z*-ratio was then determined for the crude material, and the yield and the mass balance were calculated after isolation of product and starting material.

Although there are a few differences between *o*-anisaldehyde and cinnamaldehyde, a general trend is that the Wittig reaction is fastest in methanol and slowest in THF or acetonitrile. It is also the case that the reactions in water, despite the low solubility of the reagents, are faster than all the scrutinized organic solvents except methanol. The faster the Wittig reaction proceeds, the lower the *E/Z*-selectivity observed; hence water as a medium gives somewhat lower *E/Z*-ratios than those obtained with organic solvents.

Additional Wittig reactions in water were then studied in order to determine the efficacy of this novel reaction system employing various phosphoranes and aldehydes. Excellent yields (up to 98%) and very high *E/Z*-isomeric ratios (up to 99:1) of the olefination products were obtained, particularly when aromatic carboxaldehydes were utilized (Table 2).

Water is used as a medium in the formation of products **7**−**10** in high yields (20 °C, 1 h). Particularly, water as a medium is noticeable in the formation of chalcone (**6**, entry 1) since benzaldehyde has been reported to undergo the same Wittig transformation in refluxing benzene for 3 days (entry 2).[39] Methoxycarbonylmethylenetriphenylphosphorane undergoes a rapid Wittig reaction with benzaldehyde in water at *ambient temperature* to form a high yield of methyl cinnamate (**7**) in 60 min (entry 3). As a notable comparison, when substituting water as a medium with MeOH to provide homogeneous reaction conditions, a complete conversion of benzaldehyde to product is obtained, but the *E/Z*-ratio is significantly depleted to 3:1 for cinnamate **7**. On the other hand, a considerably higher *E/Z*-ratio is obtained when employing water as a medium. Consistently high yields and *E/Z*-ratios of the Wittig reactions are obtained in water with various phosphoranes (entries 4−6). As a comparison between the efficiency of water and ionic liquids in conducting Wittig reactions, benzalacetone (**10**) has been obtained in more or less the same yield and *E/Z*-ratio either in 1.0 M solution of $[Bmim][BF_4]$[25] at 60 °C (2.5 h) or (as described herein) using water at 20 °C (1 h) (entry 6). Even though the aqueous Wittig reaction appears heterogeneous, these

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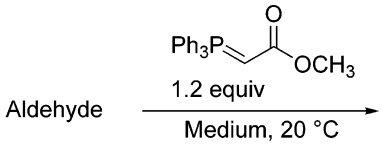
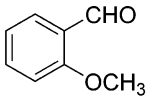
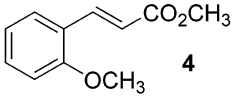
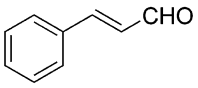
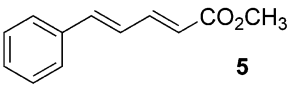
TABLE 1. Rate Study of the Wittig Reaction in Different Media[a]



Entry	Aldehyde	Medium	Time[b]	Yield[c]	*E/Z*[d]	Product
1		Water	1 h	81% (15%)	76/24	 **4**
2		Methanol	1 h	92% (5%)	65/35	
3		CH_2Cl_2	1 h	47% (48%)	81/19	
4		Toluene	1 h	36% (61%)	82/18	
5		CCl_4	1 h	25% (71%)	80/20	
6		THF	1 h	25% (71%)	84/16	
7		Acetonitrile	1 h	33% (63%)	84/16	
8		Water	2 h	88% (7%)	84/16	 **5**
9		Methanol	2 h	94% (0%)	67/33	
10		CH_2Cl_2	2 h	78% (14%)	84/16	
11		Toluene	2 h	59% (35%)	91/9	
12		CCl_4	2 h	71% (27%)	91/9	
13		THF	2 h	33% (60%)	92/8	
14		Acetonitrile	2 h	41% (55%)	90/10	

[a] The reactions were conducted on a 1 mmol scale in 5 mL of medium. [b] 5 mL of 1.0 M HCl(aq) was added after the time indicated. [c] Isolated product yield and recovered aldehyde in parenthesis. [d] Determined using ^{1}H NMR of crude reaction mixtures.

initial results demonstrate that water is a very useful component for facilitating the olefination process and does not jeopardize the *E/Z*-selectivity of the resulting alkenes (**6**−**10**).

The Wittig reaction in water is a straightforward protocol that works favorably between various ylides and countless types of aromatic carboxaldehydes having either electron-donating or electron-withdrawing groups present. In general, it is noticed that even though the solid aldehydes are rapidly stirred or vigorously mixed in water they seem to form aggregates which react more slowly with the phosphoranes in comparison to the readily dispersed liquid aldehydes in water. Therefore, distributing the aldehyde molecules more readily in water by applying heat is also an effective way of increasing the rate and the yield of the aqueous Wittig reactions. Conceivably, the rate of the hydrolysis of the phosphorus ylides with water is slower than the reaction between ylides and aldehydes. An elevated reaction temperature when using solid aldehydes such as *p*-nitro- (entry 8), *p*-cyano- (entry 10), or *p*-bromobenzaldehyde (entry 11) provides high yields of the corresponding products.

Also, in water, we observed that *p*-anisaldehyde reacts slowly with ylides (even though *p*-anisaldehyde is a liquid at 20 °C) to give 66% yield of product **15** after 4 h at 20 °C. At the same time, heating the same reaction to 90 °C for 30 min increased the yield of **15** to 90% without affecting the *E/Z*-ratio (entry 13). The effect of electron-donating groups has been previously reported to reduce the rate of the Wittig reaction in MeOH.[40] The efficiency of water as a reaction medium compared to organic solvents is evident in view of the fact that this Wittig reaction has been reported utilizing *p*-anisaldehyde and the same ylide in refluxing CH_2Cl_2 (4 h, 8%),[20a] in refluxing benzene (2 days, 73%),[20a] or in an ionic liquid at 60 °C (3 days, 82%)[25] (entries 13−15). As a comparison, the Wittig reaction conducted in water using the corresponding 3,4-methylenedioxybenzaldehyde or 3,4-dimethoxybenzaldehyde gives cinnamates **19** and

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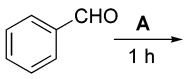
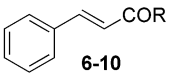
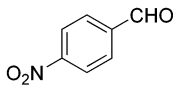
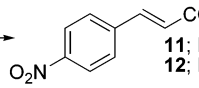
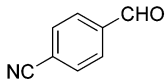
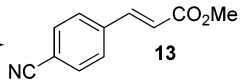
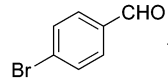
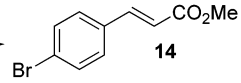
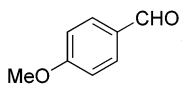
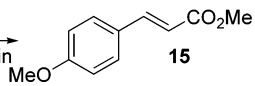
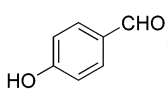
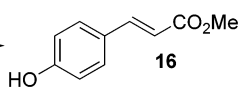
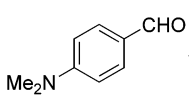
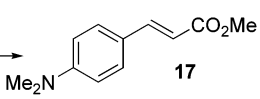
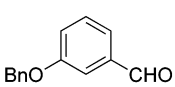
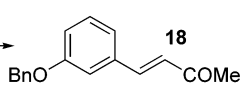
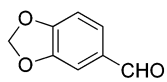
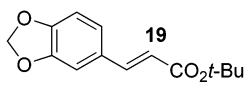
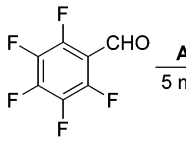
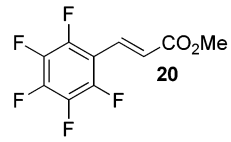
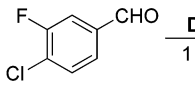
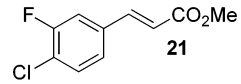
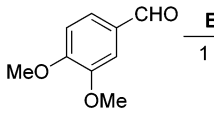
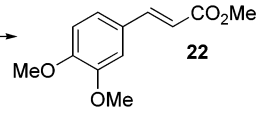
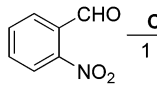
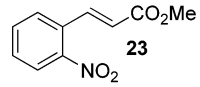
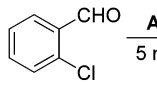
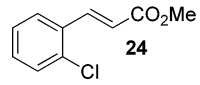
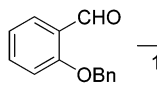
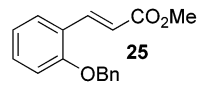
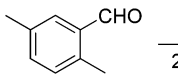
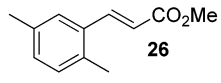
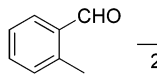
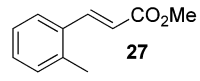
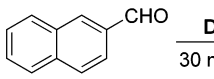
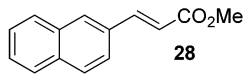
TABLE 2. Wittig Reactions of Various Aromatic Aldehydes and Stabilized Ylides in Water[a]

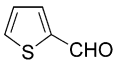
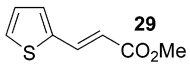
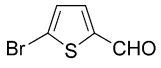
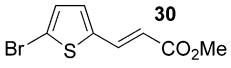
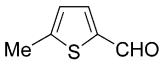
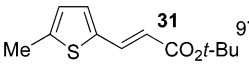
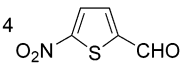
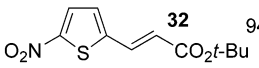
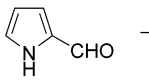
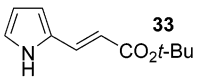
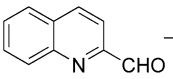
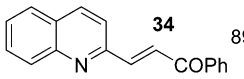
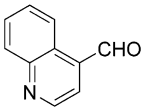
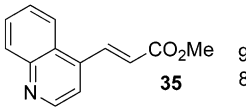
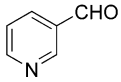
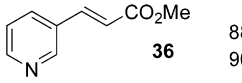
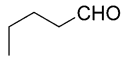
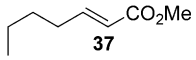
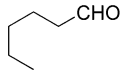
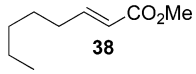
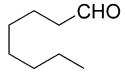
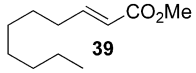
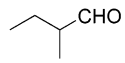
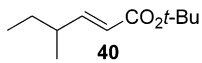
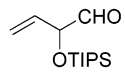
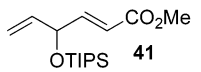
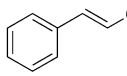
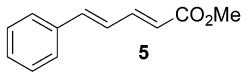
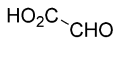
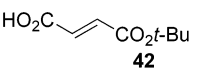
Entry	Substrate	Cond.[a]	Product	Yield (%),[b] *E*:*Z*[c]
1		A, 1 h	 **6-10**	**6**; R = Ph: 91, 90:10
2				**6**; R = Ph: 70[d]
3				**7**; R = OMe: 88, 93:7
4				**8**; R = O*t*-Bu: 97, 92:8
5				**9**; R = OTrce: 93, 94:6
6				**10**; R = Me: 85, 98:2
7				**10**; R = Me: 86[e]
8		B, 1 h	 **11**; R = Ph	93, 84:16
9			**12**; R = Me	96, 87:13
10		B, 2 h	 **13**	86, 87:13
11		B, 20 min	 **14**	78, 89:11
12				84[g]
13		C, 30 min	 **15**	90,[h] 92:8
14				8[i]
15				82[j]
16		B, 1 h	 **16**	92, 95:5
17				8[i]
18		B, 2 h	 **17**	81, 90:10
19				78,[k] 3:1
20				0[i]
21		B, 2 h	 **18**	98, 95:5
22		C, 1 h	 **19**	98, 95:5
23		A, 5 min	 **20**	86, 99:1
24		D, 1 h	 **21**	95, 96:4
25		B, 1 h	 **22**	90, 99:1
26				90[f]
27		C, 1 h	 **23**	92, 88:12
28		A, 5 min	 **24**	97, 81:19
29		C, 1 h	 **25**	91, 73:27
30		A, 2 h	 **26**	92, 94:6
31		A, 2 h	 **27**	89, 93:7
32		D, 30 min	 **28**	98, 90:10
33				98[l]

[a] The reactions were conducted on a 1 mmol scale in 5 mL of deionized water. [b] Isolated purified material. [c] Crude reaction mixtures analyzed by 500 MHz ^{1}H NMR. [d] Reflux PhH, 3 days.[39] [e] [Bmim][BF_4], 60 °C, 2.5 h.[25] [f] Reflux PhH, 12 h.[41] [g] MeOH, 30 °C, 3 h.[40a] [h] 4 h at 20 °C gave 66% **15** (*E*/*Z*-ratio: 92:8). [i] Reflux CH_2Cl_2, 4 h.[20a] [j] [Bmim][BF_4], 60 °C, 72 h.[25] [k] MeOH, 20 °C, 3 h. [l] Reflux THF, 12 h.[43] **A** = 1.2 equiv of ylide, 20 °C; **B** = 1.5 equiv of ylide, 90 °C; **C** = 1.2 equiv of ylide, 90 °C; **D** = 1.5 equiv of ylide, 20 °C; Trce = 2,2,2-trichloroethoxy.

22 in outstanding chemical yields and excellent *E*/*Z*-ratios after 1 h at 90 °C (entries 22 and 25). It is also worth noting that strong electron-donating groups (e.g., amines) can be present, hence the slowly reacting *p*-Me_2N-substituted benzaldehyde does not react with the ylide in water at 20 °C, but after 2 h at 90 °C, it affords product **17** in 81% yield (entry 18). However, when conducting this reaction in MeOH, this alternative procedure provides 78% of **17** at 20 °C after 5 h, but the *E*/*Z*-ratio is significantly diminished to 3:1 (entry 19). This lowering of *E*/*Z*-ratios appears to be a common effect of applying MeOH as a solvent. In addition, the corresponding reaction in CH_2Cl_2 (reflux 4 h)[20a] has been reported to be fruitless (entry 20), which again underscores the impact of water over CH_2Cl_2. It is also interesting that the Wittig reaction in water works well with substrates having acidic unprotected functional groups present; hence the presence of a carboxylic acid group (vide infra) or phenolic groups, such as *p*-hydroxybenzaldehyde, gives the corresponding cinnamate product **16** in 92% after heating the reaction for 1 h at 90 °C (entry 16). In sharp contrast, the same reaction in refluxing CH_2Cl_2 (4 h)[20a] has been reported to provide only 8% of **16**.

The presence of electron-withdrawing groups in the aromatic ring increases the rates of the Wittig reaction in water. At present, we are unable to draw a wider general conclusion regarding the electronic contribution of these substituents being responsible for the rate of the reaction. The aqueous Wittig reactions utilizing the pentafluorobenzaldehyde (entry 23) or the *o*-chlorobenzaldehyde (entry 28) are complete in less than 5 min at 20 °C. The *E*/*Z*-ratio of product **20** was very high (99:1) compared to the lower *E*/*Z*-ratio observed for **24** (81:19) utilizing *o*-chlorobenzaldehyde. In contrast, solid aldehydes, such as the 4-chloro-3-fluorobenzaldehyde (entry 24) or the 2-nitrobenzaldehyde (entry 27), require longer reaction time for completion in water. The observed *E*/*Z*-ratios of the products are generally slightly lower when utilizing some of the *ortho*-substituted benzaldehydes. Though the evident *ortho*-substituted

TABLE 3. Wittig Reactions of Various Aldehydes and Stabilized Ylides in Water[a]

Entry	Substrate	Cond.[a]	Product	Yield (%),[b] *E*:*Z*,[c]
1		**A**, 1 h	 **29**	95, 92:8
2		**B**, 5 min	 **30**	89, 91:9
3		**B**, 1 h	 **31**	97, 90:10
4		**C**, 1 h	 **32**	94, 86:14
5		**C**, 1 h	 **33**	84, 99:1
6		**C**, 2 h	 **34**	89, 99:1
7 8		**C**, 2 h	 **35**	92, 99:1 83[g]
9 10		**B**, 1 h	 **36**	88, 81:19 90[h]
11		**B**, 1 h	 **37**	80, 82:18
12 13		**B**, 1 h	 **38**	84, 81:19 82[d]
14 15		**B**, 1 h	 **39**	86, 80:20 93[e]
16		**B**, 1 h	 **40**	77, 99:1
17		**C**, 2 h	 **41**	83, 88:12
18 19 20		**B**, 2 h	 **5**	98, 85:15 64[f] 86[d]
21		**A**, 30 min	 **42**	74, 70:30[i]

[a] The reactions were conducted on a 1 mmol scale in 5 mL of deionized water. [b] Isolated purified material. [c] Crude reaction mixtures analyzed by 500 MHz ^{1}H NMR. [d] [Bmim][BF$_4$], 60 °C, 12 h.[25] [e] Reflux THF, 12 h.[46] [f] Reflux PhMe, 4 h.[47] [g] Reflux PhH, 19 h.[44] [h] Reflux CH_2Cl_2, 4 h.[45] [i] *E*/*Z*-ratio is sensitive to the silica gel (purification) applied; SiO_2 column gave ~50% (*E*/*Z* = 99:1). **A** = 1.0−1.2 equiv of ylide, 20 °C; **B** = 1.5 equiv of ylide, 20 °C; **C** = 1.5 equiv of ylide, 90 °C; TIPS = triisopropylsilyl.

steric effect appears to be one factor of influence, electronic effects should not be ruled out as shown below. For example, it is interesting that *o*-nitrobenzaldehyde (entry 27) and *p*-nitrobenzaldehyde (entry 9) gave roughly the same *E*/*Z*-ratios.[42] We also note that when relatively sizable electron-donating *ortho*-substituents are present, such as with the *o*-benzyloxy- or the *o*-methoxy-substituted benzaldehydes, a quite low *E*/*Z*-ratio is observed for the products (**4**, **25**) obtained in the aqueous Wittig reaction. In significant contrast, the *o*-methyl-substituted carboxaldehydes provide *E*/*Z*-ratios of up to 94:6 and good yields of up to 92% of **26** and **27**. In this case, it appears as if the methyl groups have no influence on the isomeric ratio of the products (entry 3 vs entry 31). Naphthalene-2-carboxaldehyde reacts nicely with the ylide in water giving 98% of ester **28** after applying heat for 30 min. Ester **28** has also been prepared via the same Wittig reaction in refluxing THF, but required 12 h.[43]

Extending our study to heterocyclic aromatic aldehydes (Table 3), we find that the liquid thiophenecarboxaldehydes (entries 1−3) react without difficulty with the phosphoranes in water at 20 °C.

In sharp contrast to the preceding examples that employed common aromatic carboxaldehydes, the solid heterocyclic aromatic aldehydes required heat in order to produce acceptable yields of the products when conducting Wittig reactions in water. Thus, pyrrole-, quinoline-, and pyridinecarboxaldehydes do not pose any problem and provide high yields and for the most part excellent *E*/*Z*-ratios of the corresponding products (**33**−**36**). The *E*/*Z*-ratio was modest employing 3-pyridinecarboxaldehyde (entry 9) but was exceptional when using 2- or 4-quinolinecarboxaldehyde (entries 6 and 7). Both of these aldehydes react nicely with the ylides in water giving 89% of ketone **34** and 92% of ester **35** after applying heat. As a comparison to the Wittig reactions in water, esters **35** and **36** have been synthesized in refluxing benzene for 19 h[44] or refluxing CH_2Cl_2 for 4 h,[45] respectively (entries 8 and 10).

The Wittig reaction in water is also applicable to aliphatic aldehydes (entries 11−17) where high yields of the corresponding α,β-unsaturated methyl-, *tert*-butyl-, and 2,2,2-trichloroethyl ester (**3**) are obtained by utilizing various ylides. The yields of products **37**−**39** increase as the alkyl chain for the aliphatic aldehyde is extended. In contrast, the smaller aliphatic aldehydes produce low yields of the olefination product when the Wittig

(41) Nam, N.-H.; You, Y.-J.; Kim, Y.; Hong, D.-H.; Kim, H.-M.; Ahn, B. Z. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 1173−1176.

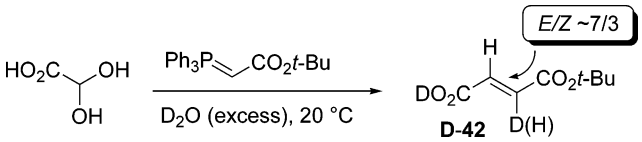
(42) See also Table 4.

(43) Hamilton, G. S.; Wu, Y.-Q.; Limburg, D. C.; Wilkinson, D. E.; Vaal, M. J.; Li, J.-H.; Thomas, C.; Huang, W.; Sauer, H.; Ross, D. T.; Soni, R.; Chen, Y.; Guo, H.; Howorth, P.; Valentine, H.; Liang, S.; Spicer, D.; Fuller, M.; Steiner, J. P. *J. Med. Chem.* **2002**, *45*, 3549−3557.

(44) Rodriguez, J. G.; Benito, Y. *J. Heterocycl. Chem.* **1988**, *25*, 819−821.

(45) Agarwal, K. C.; Knaus, E. E. *J. Heterocycl. Chem.* **1985**, *22*, 65−69.

SCHEME 2

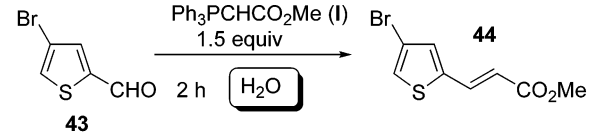


reactions were conducted in water.[48] Smaller aldehydes have a greater propensity to form hydrates with water, and as a consequence, they could be less prone to undergo the aqueous Wittig reaction. The same argument might explain the challenges employing smaller aliphatic α-substituted aldehydes. When applying relatively large α-branched aliphatic aldehydes, the yields of the Wittig products formed in water are again high. Although the aqueous Wittig reactions generally proceed more slowly when employing α-substituted aldehydes (Scheme 1), it is still possible to obtain high yields of product if the aldehydes are exposed to the ylides for a longer duration or elevated reaction temperature. For example, the very bulky α-OTIPS-substituted 3-butenealdehyde[49] (entry 17) gives high yields and *E*/*Z*-ratios of the Wittig products formed in water after heating the reaction at 90 °C for 2 h.

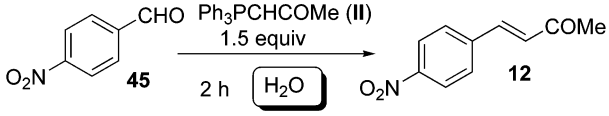
Glyoxylic acid undergoes a rapid Wittig reaction in water at 20 °C (entry 21), which is unexpected given that the aldehyde exists mainly as a hydrate in water (∼99%).[50] When following the Wittig reaction in D_2O at 20 °C (Scheme 2) using NMR, the methine signal of the hydrate of glyoxylic acid ($\delta_{CH} = 5.2$ ppm) slowly disappears in the presence of the ylide. The Wittig product (**42**) is then formed along with triphenylphosphine oxide, which makes the reaction more heterogeneous over time. NMR analysis confirmed the formation of the product, as well as the resultant incorporation of deuterium (D/H ∼ 10/1) at the α-olefinic carbon of ester **42**. In a separate experiment, it was confirmed that the proton/deuterium exchange can easily occur if there is a significant concentration of D_2O. The incorporation of the deuterium at the α-carbon is due to the basicity of the ylide prior the Wittig reaction. These results show that, even if the aldehyde molecule is masked as its hydrate, the Wittig product is still obtained.

Carrying out the Wittig reaction with glyoxylic acid unfortunately creates problems with the workup procedure. Specifically, it is a challenge to isolate and purify the major geometrical isomer of mono-*tert*-butyl fumarate (**42**). The isolated yield typically is around 50%, although the chemical yield of the reaction is much higher.[51] Isolation and purification of product **42** on a 1.2−1.5 mmol scale from triphenylphosphine oxide was best conducted using a short silica gel column. Moreover, the *trans*-**42** isomer is sensitive to acid−base extraction and partially isomerizes to the corresponding *cis*-**42** isomer (mono-*tert*-butyl maleate).

TABLE 4. Influence of Additives on the Wittig Reactions Conducted in Water[a]



Entry	Conditions	Yield (%)[b]	*E*:*Z* ratio[c]
1	20 °C	77	94:6
2	20 °C, 5% DMSO	99	94:6
3	80 °C	99	94:6
4	20 °C, $PhCO_2H$[d]	85	99:1
5	20 °C, LiCl[d]	87	94:6
6	20 °C, SDS[e]	74	91:9



Entry	Conditions	Yield (%)[b]	*E*:*Z* ratio[c]
7	20 °C	63	90:10
8	20 °C, 5% DMSO	89	80:20
9	80 °C	96	87:13
10	20 °C, $PhCO_2H$[d]	85	91:9
11	20 °C, LiCl[d]	76	92:8
12	20 °C, SDS[e]	63	89:11

[a] The reactions were conducted on a 1 mmol scale in 5 mL of deionized water. [b] Isolated purified material. [c] Crude reaction mixtures analyzed by 500 MHz ^{1}H NMR. [d] 10 mol % vs aldehyde. [e] Sodium dodecyl sulfate, 30 mol %.

Several variations on the reaction conditions of the Wittig reaction have appeared in efforts to improve the reaction outcome.[19−25] In light of the fact that additives such as lithium halides[21a,b] or benzoic acid[21c−g] and recently aqueous LiCl[26] and a surfactant[27] have been reported to improve the yield and *E*/*Z*-ratios in Wittig reactions, we investigated the influence of those additives on Wittig reactions conducted in water (Table 4).

Aldehydes **43** and **45** were exposed to ylides **I** and **II** in neat water at 20 °C. Even though the Wittig reactions are incomplete after 2 h, they provide decent yields (up to 77%) and *E*/*Z*-ratios (up to 94:6) of **44** and **12**. Since the solid aldehyde (**45**) reacts more slowly with ylides in neat water, heat was applied to the system and the yield increased accordingly (entry 9). Heating these reactions increases the yield of product but does not necessarily decrease the *E*/*Z*-ratio significantly. The presence of 5% DMSO as an additive increases the yield of the Wittig reactions in water, presumably due to the increased dispersion in the medium. Although DMSO dissolves aldehyde **45**, it does not improve the *E*/*Z*-ratio (entry 8). In contrast, water significantly influences the *E*/*Z*-ratio of product **12** (entry 7). The presence of either aqueous lithium chloride or benzoic acid influences the aqueous Wittig reaction. For example, using 10 mol % of benzoic acid relative to the aldehyde increases the yield and the *E*/*Z*-ratio of **44** (entry 4) and **12** (entry 10). The presence of LiCl (10 mol %) has a positive effect on the yield of the aqueous Wittig reactions (entries 5 and 11) but a minor influence on the *E*/*Z*-ratio. It is conceivable that LiCl has a

(46) Kandula, S. R. V.; Kumar, P. *Tetrahedron Lett.* **2003**, *44*, 6149−6151.

(47) Ramage, R.; Griffiths, G. J.; Shutt, F. E. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1531−1537.

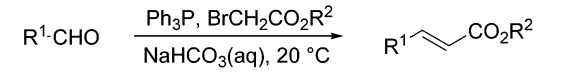
(48) Additional aldehydes scrutinized in water (yield %): pivaldehyde (0), formaldehyde (0), isobutyraldehyde (40), and cyclohexanecarboxaldehyde (24).

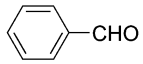
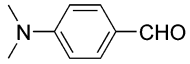
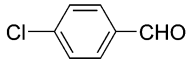
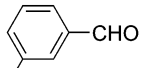
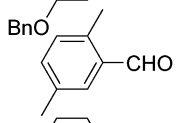
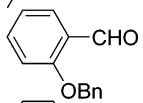
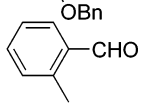
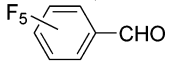
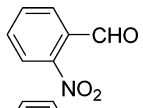
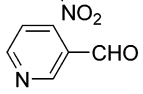
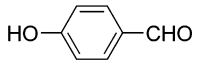
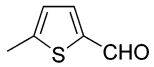
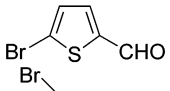
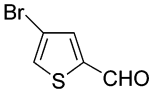
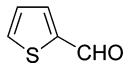
(49) For preparation of 2-hydroxy-3-butenoic acid methyl ester, see: Stach, H.; Huggenberg, W.; Hesse, M. *Helv. Chim. Acta* **1987**, *70*, 369−374. TIPS protection of the alcohol (81%) and subsequent DIBAL-H reduction in CH_2Cl_2 (90%) gave the desired aldehyde in 44% overall yield (four steps).

(50) According to NMR analysis, see also: *The Aldrich Library of ^{13}C and ^1H NMR Spectra* **1993**, *1*, 822.

(51) The reaction has previously been reported in 74% yield; see ref 13.

TABLE 5. Wittig Reactions Using Ph_3P and α-Bromoesters in Aqueous $NaHCO_3$



Entry	Aldehyde	R^2	Time	Product	Yield[b]	*E:Z*[c]
1		Et	2 h	**46**	93%	93:7
2		Bn	2 h	**47**	89%	96:4
3		Et	2 h	**48**	32%	99:1
4[d]		Et	2 h	**48**	23%	99:1
5		Et	2 h	**49**	99%	89:11
6		Bn	2 h	**50**	84%	92:8
7		Et	2 h	**51**	94%	93:7
8		Bn	2 h	**52**	86%	91:9
9		Et	2 h	**53**	99%	92:8
10		*t*-Bu	3 h	**54**	96%	93:7
11		Et	2 h	**55**	97%	92:8
12		*t*-Bu	3 h	**56**	92%	72:28
13		Bn	3 h	**57**	90%	94:6
14		Bn	2 h	**58**	82%	98:2
15		*t*-Bu	40 min	**59**	84%	98:2
16		*t*-Bu	1.5 h	**60**	99%	85:15
17		Et	1 h	**61**	81%	87:13
18		Bn	2 h	**62**	64%	94:6
19		Et	1 h	**63**	99%	93:7
20		*t*-Bu	1.5 h	**30**	99%	91:9
21		*t*-Bu	1.5 h	**64**	99%	91:9
22		Et	1 h	**65**	98%	88:12
23		*t*-Bu	1.5 h	**66**	99%	99:1
24		*t*-Bu	1.5 h	**67**	99%	92:8

[a] The reactions were conducted on a 1 mmol scale using saturated $NaHCO_3$ (5 mL), 1.4−1.5 equiv of PPh_3, and 1.6−1.8 equiv of α-bromoester. [b] Isolated purified material. [c] Crude reaction mixtures analyzed by ^1H NMR. [d] Reaction conducted at 90 °C.

stabilizing effect on the phosphoranes thus preventing the ylide from reacting with water.[26a]

The use of surfactants employing a *n*-Bu_3P/SDS mixture has been reported to slightly increase the yield in Wittig reactions,[27] but SDS was not observed to influence the yield for the aqueous reactions using either of the triphenylphosphoranes (entries 6 and 12). It is possible that SDS enhances separation of the ylide from the aldehyde, similar to an effect of an organic solvent, acting against the "hydrophobic repellent" effect of the water.

Based on the concept of preparing phosphoranes in situ during the Wittig process, we extended our work by simply mixing Ph_3P, α-bromoesters, saturated $NaHCO_3$, and aldehydes using water as the only medium. Based on the previous LiCl/LiOH combination for Wittig reactions,[26c] we now report the use of a saturated aqueous $NaHCO_3$ solution to achieve the aqueous one-pot Wittig reactions at +20 °C using Ph_3P, α-bromoesters, and aromatic carboxaldehydes (Table 5).

Triphenylphosphine (1.4−1.5 equiv), the appropriate α-bromoester (1.6−1.8 equiv), and aldehyde were charged to a saturated aqueous $NaHCO_3$ solution, and the mixture was stirred or shaken for 1−3 h at 20 °C. After adjusting the pH to ∼5.5 using sulfuric acid, isolation, purification, and characterization of the Wittig products were conducted (Table 5). The yields of product obtained from the in situ preparation of the ylides are generally excellent (82−99%), and the *E/Z*-ratios are for the most part very good (up to 99:1). Although these Wittig reactions do not require heating, the results obtained generally follow the results obtained using the phosphorus ylides in water previously presented (Tables 2 and 3). Hence the electron-donating, electron-withdrawing groups, and the location of the substituents in the ring influence the *E/Z*-ratio. The normally less reactive *p*-anisaldehyde (entry 7) and the *m*-benzyloxybenzaldehyde (entry 9) react fast in the aqueous basic media. Similarly, the *o*-benzyloxybenzaldehyde (entry 12) did not require heating and gave a decrease in the *E/Z*-ratio, as noted earlier for the phosphorus ylides (Table 2). Likewise, the *o*-substituted tolylaldehydes (entries 11 and 13) generated an increased *E/Z*-ratio under basic reaction conditions similar to the results obtained using phosphorus ylides with aldehydes in water. With the observation of the nucleophilic nitrogen substituting the bromide on the α-bromoester, it is not entirely surprising that the *p*-Me_2N-substituted benzaldehyde gave a low yield during the basic aqueous Wittig reaction (entry 3).

Several models have been proposed to explain the observed *E/Z*-product ratio and the selectivity of the Wittig reaction depending on what types of ylides are employed.[52] The model which best accounts for the experimental results was developed by Vedejs et al.[53] Along with the overwhelming corroboration for the formation of the oxaphosphetane intermediates,[52b,54] this model[53a] is based on extensive practical experimentation and on computational methodology to simulate the Wittig reaction process. Very recently, however, Aggarwal and Harvey[17] reported calculations of the transition state for the salt-free Wittig reaction of stabilized ylides. Their model explains the high

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(54) (a) Trindle, C.; Hwang, J.-T.; Carey, F. A. *J. Org. Chem.* **1973**, *38*, 2664−2669. (b) Höller, R.; Lischka, H. *J. Am. Chem. Soc.* **1980**, *102*, 4632−4635. (c) Rose, I. A. *J. Am. Chem. Soc.* **1984**, *106*, 6117−6119. (d) Volatron, F.; Eisenstein, O. *J. Am. Chem. Soc.* **1987**, *109*, 1−14. (e) Rzepa, H. S. *J. Chem. Soc., Perkin Trans. 2* **1989**, *12*, 2115−2119. (f) Mari, F.; Lahti, P. K.; McEwen, W. E. *Heteroat. Chem.* **1991**, *2*, 265−276. (g) Naito, T.; Nagase, S.; Yamataka, H. *J. Am. Chem. Soc.* **1994**, *116*, 10080−10088. (h) Restrepo-Cossio, A. A.; Cano, H.; Mari, F.; Gonzalez, C. A. *Heteroat. Chem.* **1997**, *8*, 557−569. (i) Restrepo-Cossio, A. A.; Gonzalez, C. A.; Mari, F. *J. Phys. Chem. A* **1998**, *102*, 6993−7000. (j) Lu, W. C.; Wong, N. B.; Zhang, R. Q. *Theor. Chem. Acc.* **2002**, *107*, 206−210. (k) Seth, M.; Senn, H. M.; Ziegler, T. *J. Phys. Chem. A* **2005**, *109*, 5136−5143.

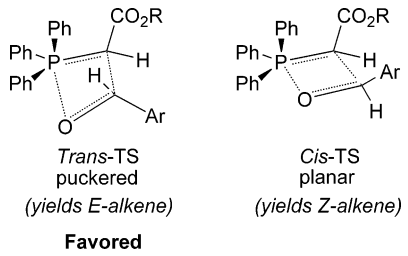

FIGURE 1. TS models to account for the *E/Z*-selectivity.

E-selectivity of product using a stabilized ylide by the considerably puckered oxaphosphetane-type transition state (Figure 1).

From our rate study conducted in various solvents (Table 1), the Wittig reactions conducted in protic media, such as methanol and water, give slightly lower *E*-selectivity for the *o*-alkoxy-substituted aromatic aldehydes compared to *p*-alkoxy-substituted aldehydes. However, the *E/Z*-ratios vary over a rather narrow range, and the observed effects could be consistent with more than one proposed enhancement mechanism. Although it is suspected that water molecules lower the energy of the transition state for the Wittig reaction, the exact role of water in accelerating the rate of the Wittig reactions is still not clear.

Conclusions

The desire to use water as a "solvent" in organic chemistry[55] stems from the fact that water is extremely inexpensive and easy to handle and represents no environmental concerns. Although the *hydrophobic effect*[5,56] is instrumental in biological systems, water has been generally ignored in organic reactions, due to solubility problems and its amphoteric nature. However, gradually increasing interest in aqueous organic reactions has been apparent, dating from the work of Breslow[1] and Grieco[2] to more recent studies by Sharpless[4,37] and Nicolaou.[12] Extending this methodology to a fundamental alkene synthesis, we report here the enhancement of reactivity in Wittig reactions by water, perhaps due to its ability to stabilize the polar transition state of the reaction. Water may also be disposed to participate in the Wittig reaction based on its protic nature.

Water has been shown to be an effective medium for the Wittig reaction employing stabilized ylides or in situ formed stabilized ylides and aldehydes. This work demonstrates that water solubility of the reagents and substrates is not essential, even when pronounced hydrophobic entities are present. These results further support the suggestion that water should be routinely considered as a medium for organic synthesis, for reasons both of environmental consideration and of chemical efficacy.

Experimental Section

Typical Procedure for Wittig Reactions Using Aldehydes and Ylides in Water. Preparation of Compounds 2−42, 44. A 20 mL scintillation vial, fitted with a magnetic stir bar, was charged with ylide (1.2−1.5 mmol), the appropriate aldehyde (1.0 mmol), and deionized water (5.0 mL). The vial was capped, and the content was stirred, alternatively shaken, for 1−4 h. Optionally, the vial was heated to 80−90 °C at 1 atm for a maximum of 2 h. After cooling the heterogeneous reaction mixture to +20 °C, the aqueous phase was extracted with CH_2Cl_2 (3 × 5 mL) and the combined organic layers were dried over $MgSO_4$. After removal of the solvent, the crude material was dried and the *E/Z*-ratio was determined using ^{1}H NMR spectroscopy. The crude product was subsequently purified using chromatography on a silica gel column. The crude material was purified by flash chromatography employing silica gel 60 Å. The yield was determined on >98% pure products.

Typical Procedure for Wittig Reactions in Aqueous Sodium Bicarbonate Using Aldehydes, α-Bromoesters, and Triphenylphosphine. Preparation of Compounds 46−67. A 20 mL scintillation vial, fitted with a magnetic stir bar, was charged with triphenylphosphine (1.4−1.5 mmol), saturated aqueous $NaHCO_3$ (5.0 mL), appropriate α-bromoester (1.6−1.8 mmol), and aldehyde (1.0 mmol). The vial was capped, and the content was stirred, alternatively shaken, for 1−4 h, and the pH was adjusted to ∼5.5 using sulfuric acid (1.0 M). Isolation, purification, and characterization of the Wittig product were conducted as indicated above.

5(*R*)-(*tert*-Butyldimethylsilyloxy)-4(*R*),6-dimethyl-2(*E*)-heptenoic acid methyl ester (2).[35] **2** was obtained from a Wittig reaction between aldehyde **1**[35] (0.307 mmol, 75 mg) and (methoxycarbonylmethylene)triphenylphosphorane (0.553 mmol, 184 mg) in water (3 mL) at 90 °C for 2 h. The crude product was purified using flash chromatography (2.5% Et_2O/pentane, R_f 0.30) to give 67% (62 mg) of **2** as a clear oil (*E/Z*-ratio: 87/13): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.00 (dd, CH^{β}═CH$^{\alpha}$, J = 15.8, 7.8 Hz, 1H), 5.79 (dd, CH$^{\beta}$═CH^{α}, J = 15.8, 1.3 Hz, 1H), 3.73 (s, OCH_3, 3H), 3.38 (dd, OC*H*, J = 4.8 Hz, 1H), 2.51 (m, C*H*−CH═CH, 1H), 1.72 (m, C*H*$(CH_3)_2$, 3H), 1.05 (d, CH_3−CH, J = 6.7 Hz, 3H), 0.91 (s, $(CH_3)_3$-Si, 9H), 0.89 (d, CH_3−CH, J = 6.8 Hz, 3H), 0.85 (d, CH_3−CH, J = 6.7 Hz, 3H), 0.05, 0.03 (2s, CH_3−Si, 3H each); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.2, 153.3, 119.7, 80.1, 51.4, 41.0, 32.0, 26.1, 20.3, 18.4, 17.6, 15.1, −3.7, −3.8; FTIR (film, cm^{-1}) 1728, 1254, 1055. HRMS (EI, DCI/NH_3) calcd for $[C_{16}H_{33}O_3Si]^+$ 301.2199, found 301.2197.

5(*R*)-(*tert*-Butyldimethylsilyloxy)-4(*R*),6-dimethyl-2(*E*)-heptenoic acid 2′,2′,2′-trichloroethyl ester (3). 3 was obtained from a Wittig reaction between aldehyde **1**[35] (0.615 mmol, 150 mg) and (2,2,2-trichloroethoxycarbonylmethylene)triphenylphosphorane[57] (0.992 mmol, 416 mg) in water (5.0 mL) at 20 °C for 18 h. The crude product was purified using flash chromatography (2.5% Et_2O/pentane, R_f 0.40) to give 73% (189 mg) of **3** as a clear oil (*E/Z*-ratio: 85/15): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (dd, CH^{β}═CH$^{\alpha}$, J = 15.9, 7.3 Hz, 1H), 5.89 (dd, CH$^{\beta}$═CH^{α}, J = 15.9, 1.2 Hz, 1H), 4.82 (d, OCH_2, J = 12.0 Hz, 1H), 4.79 (d, OCH_2, J = 12.0 Hz, 1H), 3.44 (dd, OC*H*, J = 4.8, 4.8 Hz, 1H), 2.58 (m, C*H*CH_3, 1H), 1.75 (m, C*H*$(CH_3)_2$, 1H), 1.09 (d, CH_3−CH, J = 6.7 Hz, 3H), 0.92 (s, $(CH_3)_3$Si, 9H), 0.91 (d, CH_3-CH "partly hidden", J = 6.8 Hz, 3H), 0.86 (d, CH_3−CH, J = 6.8 Hz, 3H), 0.06, 0.05 (2s, CH_3−Si, 3H each); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.8, 156.0, 118.5, 79.9, 74.0, 41.2, 31.9, 26.2, 26.1, 20.4, 18.4, 17.8, 14.4, −3.7, −3.9; FTIR (film, cm^{-1}) 1738, 1650, 1253, 838; MS *m*/*z* 419 (M + 2, 2%), 417 (M$^+$, 4%), 401 (35%), 359 (100%), 287 (30%), 187 (85%).

3-(2′-Methoxyphenyl)-(*E*)-propenoic acid methyl ester (4).[58] Typical procedure (Table 1): **4** was obtained from a Wittig reaction between 2-methoxybenzaldehyde (0.9 mmol, 122 mg) and (methoxycarbonylmethylene)triphenylphosphorane (1.1 mmol, 366 mg) in water (4.0 mL) at 20 °C. After 1 h, CH_2Cl_2 (5 mL) was added and the reaction was quenched by the addition of 1 M HCl (2.0 mL). The mixture was shaken or stirred vigorously for an additional 5 min, and the organic layer was separated. The aqueous phase was extracted with CH_2Cl_2 (3 × 2 mL), and the combined organic layers were dried over $MgSO_4$, filtered, and evaporated. The crude material was transferred to a silica column (2 × 8 cm), and the product (**4**, 81%) and recovered aldehyde (9%) were collected as

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one fraction using flash chromatography (20% EtOAc/hexane, R_f 0.50) (*E/Z*-ratio: 76/24): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, C*H*$^\beta$=CH$^\alpha$, J = 16.2 Hz, 1H), 7.50 (dd, aromatic, J = 7.7, 1.7 Hz, 1H), 7.35 (m, aromatic, 1H), 6.98−6.92 (2m, aromatic, 2H), 6.53 (d, CH$^\beta$=C*H*$^\alpha$, J = 16.2 Hz, 1H), 3.89, 3.80 (2s, OC*H*$_3$, 3H each); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.9, 158.4, 140.3, 131.5, 128.9, 123.5, 120.7, 118.4, 111.2, 55.5, 51.6; FTIR (CH_2Cl_2, cm^{-1}) 1712, 1633, 1198, 909, 734; MS *m/z* 192 (M$^+$, 10%), 161 (M − OMe, 100%).

5-Phenyl-2(*E*),4(*E*)-pentadienoic acid methyl ester (5).[59] **5** was obtained from a Wittig reaction between cinnamaldehyde (1.0 mmol, 126 μL) and (methoxycarbonylmethylene)triphenylphosphorane (1.5 mmol, 502 mg) in water (5.0 mL) at 20 °C for 2 h. The crude product was purified using flash chromatography (15% Et_2O/pentane, R_f 0.50) to give 98% (184 mg) of **5** as a white solid; mp 64−67 °C (*E/Z*-ratio: 85/15): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48−7.43 (m, aromatic and olefinic, 3H), 7.35, 7.30 (2m, aromatic and olefinic, 3H), 6.92−6.84 (m, olefinic, 2H), 5.99 (d, olefinic, J = 15.3 Hz, 1H), 3.77 (s, OC*H*$_3$, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.5, 144.8, 140.6, 136.0, 129.1, 128.8, 127.2, 126.2, 120.8, 51.6; FTIR (CH_2Cl_2, cm^{-1}) 1716, 1628, 996, 760.

3-Phenyl-(*E*)-propenoic acid 2′,2′,2′-trichloroethyl ester (9).[60] **9** was obtained from a Wittig reaction between benzaldehyde (1.0 mmol, 102 μL) and (2,2,2-trichloroethoxycarbonylmethylene)-triphenylphosphorane[57] (1.2 mmol, 540 mg) in water (5.0 mL) at 20 °C for 1 h. The crude product was purified using flash chromatography (15% Et_2O/pentane, R_f 0.70) to give 93% (258 mg) of **9** as a clear oil (*E/Z*-ratio: 94/6): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, C*H*$^\beta$=CH$^\alpha$, J = 16.0 Hz, 1H), 7.57 (m, aromatic, 2H), 7.41 (m, aromatic, 3H), 6.54 (d, CH$^\beta$=C*H*$^\alpha$, J = 16.0 Hz, 1H), 4.88 (s, OC*H*$_2$, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.2, 147.1, 134.0, 130.9, 129.0, 128.4, 116.4, 95.2, 74.1; FTIR (film, cm^{-1}) 1732, 1635, 1450, 1307, 1148, 766, 707. HRMS (EI, DCI) calcd for [$C_{11}H_9O_2Cl_3$] 277.9668, found 277.9660.

4-(4′-Nitrophenyl)-3(*E*)-buten-2-one (12).[61] **12** was obtained from a Wittig reaction between 4-nitrobenzaldehyde (1.0 mmol, 151 mg) and (methylcarbonylmethylene)triphenylphosphorane (1.5 mmol, 478 mg) in water (5.0 mL) at 90 °C for 2 h. The crude product was purified using flash chromatography (10% EtOAc/hexane, R_f 0.40) to give 96% (183 mg) of **12** as a yellow solid; mp 101−106 °C (*E/Z*-ratio: 87/13) {lit.[61] mp 104−105 °C}: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (m, aromatic, 2H), 7.70 (m, aromatic, 2H), 7.52 (d, C*H*$^\beta$=CH$^\alpha$, J = 16.3 Hz, 1H), 6.81 (d, CH$^\beta$=C*H*$^\alpha$, J = 16.3 Hz, 1H), 2.42 (s, C*H*$_3$CO, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.4, 148.6, 140.7, 140.0, 130.4, 128.8, 124,2, 28.0; FTIR ($CHCl_3$, cm^{-1}) 1675, 1523, 1347, 735.

3-(4′-Cyanophenyl)-(*E*)-propenoic acid methyl ester (13).[62] **13** was obtained from a Wittig reaction between 4-cyanobenzaldehyde (1.0 mmol, 131 mg) and (methoxycarbonylmethylene)triphenylphosphorane (1.5 mmol, 502 mg) in water (5.0 mL) at 90 °C for 2 h. The crude product was purified using flash chromatography (10% EtOAc/hexane, R_f 0.40) to give 86% (161 mg) of **13** as a white solid; mp 98−103 °C (*E/Z*-ratio: 87/13): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70−7.59 (multiplets, aromatic and olefinic, 5H), 6.52 (d, CH$^\beta$=C*H*$^\alpha$, J = 16.0 Hz, 1H), 3.83 (s, OC*H*$_3$, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 142.3, 138.6, 132.6, 128.3, 121.4, 118.2, 113.4, 51.9; FTIR ($CHCl_3$, cm^{-1}) 1720, 1641, 731.

3-(4′-Bromophenyl)-(*E*)-propenoic acid methyl ester (14).[59] **14** was obtained from a Wittig reaction between 4-bromobenzaldehyde (1.0 mmol, 185 mg) and (methoxycarbonylmethylene)-triphenylphosphorane (1.5 mmol, 502 mg) in water (5.0 mL) at 90 °C for 20 min. The crude product was purified using flash chromatography (15% Et_2O/pentane, R_f 0.40) to give 78% (187 mg) of **14** as a white solid; mp 77−83 °C (*E/Z*-ratio: 89/11): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, C*H*$^\beta$=CH$^\alpha$, J = 16.0 Hz, 1H), 7.51 (m, aromatic, 2H), 7.37 (m, aromatic, 2H), 6.42 (d, CH$^\beta$=C*H*$^\alpha$, J = 16.0 Hz, 1H), 3.80 (s, OC*H*$_3$, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.1, 143.4, 132.1, 129.4, 124.5, 118,5, 51.7; FTIR (CH_2Cl_2, cm^{-1}) 1715, 1636, 836.

3-(4′-Methoxyphenyl)-(*E*)-propenoic acid methyl ester (15).[63] **15** was obtained from a Wittig reaction between 4-methoxybenzaldehyde (1.0 mmol, 121 μL) and (methoxycarbonylmethylene)-triphenylphosphorane (1.2 mmol, 400 mg) in water (5.0 mL) at 90 °C for 30 min. The crude product was purified using flash chromatography (15% ether/pentane, R_f 0.40) to give 90% (172 mg) of **15** as a white solid; mp 76−80 °C (*E/Z*-ratio: 92/8): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, C*H*$^\beta$=CH$^\alpha$, J = 16.0 Hz, 1H), 7.44 (m, aromatic, 2H), 6.88 (m, aromatic, 2H), 6.29 (d, CH$^\beta$=C*H*$^\alpha$, J = 16.0 Hz, 1H), 3.80, 3.77 (2s, OC*H*$_3$, 3H each); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.5, 161.3, 144.3, 129.6, 127.0, 115.2, 114.2, 55.2, 51.3; FTIR ($CHCl_3$, cm^{-1}) 1719, 1639, 1178, 823.

3-(4′-Hydroxyphenyl)-(*E*)-propenoic acid methyl ester (16).[64] **16** was obtained from a Wittig reaction between 4-hydroxybenzaldehyde (1.0 mmol, 122 mg) and (methoxycarbonylmethylene)-triphenylphosphorane (1.5 mmol, 502 mg) in water (5.0 mL) at 90 °C for 1 h. The crude product was purified using flash chromatography (20% EtOAc/hexane, R_f 0.40) to give 92% (163 mg) of **16** as a white solid; mp 128−133 °C (*E/Z*-ratio: 95/5): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, C*H*$^\beta$=CH$^\alpha$, J = 16.0 Hz, 1H), 7.42 (m, aromatic, 2H), 6.86 (m, aromatic, 2H), 6.30 (d, CH$^\beta$=C*H*$^\alpha$, J = 16.0 Hz, 1H), 6.06 (br s, *H*OAr, 1H), 3.80 (s, OC*H*$_3$, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.2, 158.0, 144.9, 130.0, 127.1, 115.9, 115.0, 51.8; FTIR (CH_2Cl_2, cm^{-1}) 3385, 1686, 1634, 1265, 739.

3-(4′-Dimethylaminophenyl)-(*E*)-propenoic acid methyl ester (17).[65] **17** was obtained from a Wittig reaction between 4-dimethylaminobenzaldehyde (1.0 mmol, 149 mg) and (methoxycarbonylmethylene)triphenylphosphorane (1.5 mmol, 502 mg) in water (5.0 mL) at 90 °C for 2 h. The crude product was purified using flash chromatography (10% EtOAc/hexane, R_f 0.40) to give 81% (166 mg) of **17** as a yellow solid; mp 132−135 °C (*E/Z*-ratio: 90/10) {lit.[65] mp 134−135 °C}: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, C*H*$^\beta$=CH$^\alpha$, J = 15.9 Hz, 1H), 7.41 (m, aromatic, 2H), 6.66 (m, aromatic, 2H), 6.22 (d, CH$^\beta$=C*H*$^\alpha$, J = 15.9 Hz, 1H), 3.77 (s, OC*H*$_3$, 3H), 3.01 (s, $(CH_3)_2$N, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 151.8, 145.4, 129.8, 122.3, 112.2, 111.9, 51.4, 40.1; FTIR (CH_2Cl_2, cm^{-1}) 1701, 1600, 1265, 735.

4-(3′-Benzyloxyphenyl)-3(*E*)-buten-2-one (18). 18 was obtained from a Wittig reaction between 3-benzyloxybenzaldehyde (1.0 mmol, 212 mg) and (methylcarbonylmethylene)triphenylphosphorane (1.5 mmol, 478 mg) in water (5.0 mL) at 90 °C for 2 h. The crude product was purified using flash chromatography (10% EtOAc/hexane, R_f 0.40) to give 98% (247 mg) of **18** as a clear oil (*E/Z*-ratio: 95/5): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, C*H*$^\beta$=CH$^\alpha$, J = 16.2 Hz, 1H), 7.45−7.42 (m, aromatic "partly hidden", 2H), 7.42−7.37 (m, aromatic, 2H), 7.36−7.29 (m, aromatic, 2H), 7.16−7.13 (m, aromatic, 2H), 7.02 (m, aromatic, 1H), 6.68 (d, CH$^\beta$=C*H*$^\alpha$, J = 16.2 Hz, 1H), 5.09 (s, OC*H*$_2$Ph, 2H), 2.37 (s, C*H*$_3$O, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 198.3, 159.2, 143.3, 136.7, 135.9, 130.0, 128.7, 128.1, 127.50, 127.47, 121.3, 117.3, 114.2, 70.2, 27.5; FTIR (film, cm^{-1}) 1669, 1610, 1257, 697. Anal. Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 80.55; H, 6.59.

3-(3′,4′-Methylenedioxyphenyl)-(*E*)-propenoic acid *tert*-butyl ester (19). 19 was obtained from a Wittig reaction between 3,4-methylenedioxybenzaldehyde (1.04 mmol, 156 mg) and (*tert*-butoxycarbonylmethylene)triphenylphosphorane (1.2 mmol, 452

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mg) in water (5.0 mL) at 90 °C for 1 h. The crude product was purified using flash chromatography (20% EtOAc/hexane, R_f 0.60) to give 98% (253 mg) of **19** as a white solid; mp 73−76 °C (*E*/*Z*-ratio: 95/5): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, CH^{β}═CH$^{\alpha}$, J = 15.9 Hz, 1H), 7.01 (d, aromatic, J = 1.7 Hz, 1H), 6.97 (dd, aromatic, J = 8.0, 1.7 Hz, 1H), 6.79 (d, aromatic, J = 8.0 Hz, 1H), 6.19 (d, CH$^{\beta}$═CH^{α}, J = 15.9 Hz, 1H), 5.98 (s, OCH_2O, 2H), 1.52 (s, C(CH_3)$_3$, 9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 166.4, 149.3, 148.3, 143.2, 129.1, 124.0, 118.2, 108.5, 106.5, 101.4, 80.3, 28.2; FTIR (CH_2Cl_2, cm^{-1}) 1702, 1631, 1151, 800. Anal. Calcd for $C_{14}H_{16}O_2$: C, 67.73; H, 6.50. Found: C, 67.54; H, 6.89.

3-(Pentafluorophenyl)-(*E*)-propenoic acid methyl ester (20).[66] **20** was obtained from a Wittig reaction between pentafluorobenzaldehyde (1.02 mmol, 199 mg) and (methoxycarbonylmethylene)-triphenylphosphorane (1.2 mmol, 400 mg) in water (5.0 mL) at 20 °C for 5 min. The crude product was purified using flash chromatography (20% EtOAc/hexane, R_f 0.56) to give 86% (220 mg) of **20** as a clear oil (*E*/*Z*−ratio: 99/1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, CH^{β}═CH$^{\alpha}$, J = 16.5 Hz, 1H), 6.74 (d, CH$^{\beta}$═CH^{α}, J = 16.5 Hz, 1H), 3.84 (s, OCH_3, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 166.3, 145.7, 141.7, 137.8, 128.3, 125.9, 109.9, 52.0; ^{19}F NMR (188 MHz, $CDCl_3$) δ −141.0, −152.6, −163.0; FTIR (film, cm^{-1}) 1726, 1651, 1523, 1200, 737.

3-(4′-Chloro-3′-fluorophenyl)-(*E*)-propenoic acid methyl ester (21). 21 was obtained from a Wittig reaction between 4-chloro-3-fluorobenzaldehyde (1.0 mmol, 118 μL) and (methoxycarbonylmethylene)triphenylphosphorane (1.5 mmol, 502 mg) in water (5.0 mL) at 20 °C for 1 h. The crude product was purified using flash chromatography (20% EtOAc/hexane, R_f 0.50) to give 95% (204 mg) of **21** as a white solid; mp 91−94 °C (*E*/*Z*-ratio: 96/4): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, CH^{β}═CH$^{\alpha}$, J = 16.0 Hz, 1H), 7.41 (dd, aromatic, J = 8.3, 8.0 Hz, 1H), 7.29 (dd, aromatic, J = 9.8, 2.0 Hz, 1H), 7.23 (dd, aromatic, J = 8.3, 2.0 Hz, 1H), 6.41 (d, CH$^{\beta}$═CH^{α}, J = 16.0 Hz, 1H), 3.82 (s, OCH_3, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.8, 158.3, 142.3, 135.0, 131.1, 124.5, 122.9, 119.8, 115.4, 51.9; ^{19}F NMR (188 MHz, $CDCl_3$) δ −115.9; FTIR ($CHCl_3$, cm^{-1}) 1717, 1644, 1266, 739; MS *m*/*z* 216 (M + 2, 20%), 214 (M$^+$, 60%), 183 (M − OCH_3, 100%), 155 (M − CO_2CH_3, 40%). Anal. Calcd for $C_{10}H_8ClFO_2$: C, 55.96; H, 3.76. Found: C, 55.61; H, 4.07.

3-(3′,4′-Dimethoxyphenyl)-(*E*)-propenoic acid methyl ester (22).[67] **22** was obtained from a Wittig reaction between 3,4-dimethoxybenzaldehyde (1.0 mmol, 166 mg) and (methoxycarbonylmethylene)triphenylphosphorane (1.5 mmol, 502 mg) in water (5.0 mL) at 90 °C for 1 h. The crude product was purified using flash chromatography (20% EtOAc/hexane, R_f 0.20) to give 90% (200 mg) of **22** as a clear oil (*E*/*Z*-ratio: 99/1): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, CH^{β}═CH$^{\alpha}$, J = 15.9 Hz, 1H), 7.10 (dd, aromatic, J = 8.3, 2.0 Hz, 1H), 7.04 (d, aromatic, J = 2.0 Hz, 1H), 6.86 (d, aromatic, J = 8.3 Hz, 1H), 6.30 (d, CH$^{\beta}$═CH^{α}, J = 15.9 Hz, 1H), 3.90 (br s, OCH_3, 2 × 3H), 3.79 (s, OCH_3, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.6, 151.2, 149.2, 144.7, 127.4, 122.5, 115.5, 111.1, 109.8, 55.94, 55.87, 51.5; FTIR (film, cm^{-1}) 1713, 1636, 1514, 1259, 808.

3-(2′-Nitrophenyl)-(*E*)-propenoic acid methyl ester (23).[68] **23** was obtained from a Wittig reaction between 2-nitrobenzaldehyde (1.0 mmol, 151 mg) and (methoxycarbonylmethylene)triphenylphosphorane (1.2 mmol, 400 mg) in water (5.0 mL) at 90 °C for 1 h. The crude product was purified using flash chromatography (20% EtOAc/hexane, R_f 0.30) to give 92% (190 mg) of **23** as a light yellow oil (*E*/*Z*-ratio: 88/12): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (d, CH^{β}═CH$^{\alpha}$, J = 15.9 Hz, 1H), 8.03 (dd, aromatic, J = 8.5, 1.1 Hz, 1H), 7.66 (m, aromatic, 2H), 7.56 (m, aromatic, 1H), 6.37 (d, CH$^{\beta}$═CH^{α}, J = 15.9 Hz, 1H), 3.82 (s, OCH_3, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.0, 139.9, 133.4, 130.3, 130.2, 129.0, 124.8, 122.7, 51.8; FTIR (film, cm^{-1}) 1718, 1522, 1348, 757.

3-(2′-Chlorophenyl)-(*E*)-propenoic acid methyl ester (24).[69] **24** was obtained from a Wittig reaction between 2-chlorobenzaldehyde (1.05 mmol, 148 mg) and (methoxycarbonylmethylene)-triphenylphosphorane (1.2 mmol, 400 mg) in water (5.0 mL) at 20 °C for 5 min. The crude product was purified using flash chromatography (20% EtOAc/hexane, R_f 0.52) to give 97% (200 mg) of **24** as a yellow oil (*E*/*Z*-ratio: 81/19): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, CH^{β}═CH$^{\alpha}$, J = 16.0 Hz, 1H), 7.59 (dd, aromatic, J = 7.4, 2.1 Hz, 1H), 7.39 (m, aromatic, 1H), 7.30−7.23 (m, aromatic, 2H), 6.42 (d, CH$^{\beta}$═CH^{α}, J = 16.0 Hz, 1H), 3.81 (s, OCH_3, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.8, 140.5, 134.8, 132.6, 130.9, 130.1, 127.6, 127.0, 120.4, 51.7; FTIR (film, cm^{-1}) 1721, 1636, 761.

3-(2′-Benzyloxyphenyl)-(*E*)-propenoic acid methyl ester (25). 25 was obtained from a Wittig reaction between 2-benzyloxybenzaldehyde (1.1 mmol, 234 mg) and (methoxycarbonylmethylene)-triphenylphosphorane (1.2 mmol, 400 mg) in water (5.0 mL) at 90 °C for 1 h. The crude product was purified using flash chromatography (20% EtOAc/hexane, R_f 0.60) to give 91% (268 mg) of **25** as a clear oil (*E*/*Z*-ratio: 73/27): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, CH^{β}═CH$^{\alpha}$, J = 16.2 Hz, 1H), 7.48 (dd, aromatic, J = 7.7, 1.6 Hz, 1H), 7.40−7.31 (m, aromatic, 4H), 7.30−7.21 (m, aromatic, 2H), 6.94−6.86 (m, aromatic, 2H), 6.52 (d, CH$^{\beta}$═CH^{α}, J = 16.2 Hz, 1H), 5.08 (s, OCH_2Ph, 2H), 3.73 (s, OC*H*3, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 167.6, 157.2, 134.0, 136.4, 131.2, 128.7, 128.5, 127.8, 127.0, 123.7, 120.9, 118.3, 112.7, 70.2, 51.3; FTIR (film, cm^{-1}) 1715, 1632, 1170, 735; MS *m*/*z* 269 (M + 1, 55%), 268 (M$^+$, 30%), 237 (M − OCH_3, 65%), 208 (100%), 91 (30%).

3-(2′,5-Dimethylphenyl)-(*E*)-propenoic acid methyl ester (26).[70] **26** was obtained from a Wittig reaction between 2,5-dimethylbenzaldehyde (1.0 mmol, 141 μL) and (methoxycarbonylmethylene)-triphenylphosphorane (1.2 mmol, 400 mg) in water (5.0 mL) at 20 °C for 2 h. The crude product was purified using flash chromatography (10% EtOAc/hexane, R_f 0.47) to give 92% (175 mg) of **26** as a clear oil (*E*/*Z*-ratio: 94/6): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, CH^{β}═CH$^{\alpha}$, J = 15.9 Hz, 1H), 7.34 (s, aromatic, 1H), 7.07 (m, aromatic, 2H), 6.34 (d, CH$^{\beta}$═CH^{α}, J = 15.9 Hz, 1H), 3.80 (s, OCH_3, 3H), 2.38, 2.31 (2s, CH_3Ar, 3H each); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.4, 142.6, 135.7, 134.6, 133.1, 130.8, 130.7, 126.9, 118.5, 51.5, 20.8, 19.2.

3-(2′-Methylphenyl)-(*E*)-propenoic acid methyl ester (27).[71] **27** was obtained from a Wittig reaction between 2-methylbenzaldehyde (1.0 mmol, 116 μL) and (methoxycarbonylmethylene)-triphenylphosphorane (1.2 mmol, 400 mg) in water (5.0 mL) at 20 °C for 2 h. The crude product was purified using flash chromatography (10% EtOAc/hexane, R_f 0.44) to give 89% (157 mg) of **27** as a clear liquid (*E*/*Z*-ratio: 93/7): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, CH^{β}═CH$^{\alpha}$, J = 15.9 Hz, 1H), 7.53 (d, aromatic, J = 7.4 Hz, 1H), 7.29−7.23 (m, aromatic, 1H), 7.22−7.16 (m, aromatic, 2H), 6.35 (d, CH$^{\beta}$═CH^{α}, J = 15.9 Hz, 1H), 3.80 (s, OCH_3, 3H), 2.43 (s, CH_3Ar, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.4, 142.5, 137.6, 133.4, 130.8, 130.0, 126.39, 126.31, 118.9, 51.6, 19.7.

3-(2′-Naphthyl)-(*E*)-propenoic acid methyl ester (28).[72] **28** was obtained from a Wittig reaction between naphthyl-2-carboxaldehyde

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(1.0 mmol, 156 mg) and (methoxycarbonylmethylene)triphenylphosphorane (1.5 mmol, 502 mg) in water (5.0 mL) at 90 °C for 30 min. The crude product was purified using flash chromatography (20% EtOAc/hexane, R_f 0.40) to give 98% (210 mg) of **28** as a white solid; mp 79−83 °C (*E*/*Z*-ratio: 90/10): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (br s, aromatic, 1H), 7.86−7.79 (m, aromatic "*partly hidden*", 3H), 7.85 (d, C*H*$^{\beta}$=CH$^{\alpha}$ "*partly hidden*", J = 16.0 Hz, 1H), 7.65 (dd, aromatic, J = 8.6, 1.6 Hz, 1H), 7.52−7.46 (m, aromatic, 2H), 6.54 (d, C*H*$^{\beta}$=CH$^{\alpha}$, J = 16.0 Hz, 1H), 3.83 (s, OC*H*$_3$, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 167.5, 144,9, 134.3, 133.3, 131.9, 129.9, 128.7, 128.6, 127.8, 127.2, 126.7, 123.5, 118.0, 51.7; FTIR (CH_2Cl_2, cm^{-1}) 1716, 1638, 1265, 739.

3-(2′-Thiophenyl)-(*E*)-propenoic acid methyl ester (29).[73] **29** was obtained from a Wittig reaction between 2-thiophenecarboxaldehyde (1.0 mmol, 94 μL) and (methoxycarbonylmethylene)-triphenylphosphorane (1.2 mmol, 400 mg) in water (5.0 mL) at 20 °C for 1 h. The crude product was purified using flash chromatography (15% Et_2O/pentane, R_f 0.40) to give 95% (160 mg) of **29** as a light yellow solid; mp 45−47 °C (*E*/*Z*-ratio: 92/8): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, C*H*$^{\beta}$=CH$^{\alpha}$, J = 15.7 Hz, 1H), 7.36 (d, aromatic, J = 5.1 Hz, 1H), 7.25 (d, aromatic, J = 3.6 Hz, 1H), 7.04 (dd, aromatic, J = 5.1, 3.6 Hz, 1H), 6.24 (d, CH$^{\beta}$=C*H*$^{\alpha}$, J = 15.7 Hz, 1H), 3.79 (s, OC*H*$_3$, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.2, 139.5, 137.2, 130.9, 128.4, 128.1, 116.6, 51.6; FTIR (CH_2Cl_2, cm^{-1}) 1701, 1635, 1205, 742. HRMS (DEI) calcd for [$C_8H_8O_2S$] 168.0245, found 168.0241.

3-(5′-Bromo-2′-thiophenyl)-(*E*)-propenoic acid methyl ester (30). 30 was obtained from a Wittig reaction between 5-bromothiophene-2-carboxaldehyde (1.0 mmol, 119 μL) and (methoxycarbonylmethylene)triphenylphosphorane (1.5 mmol, 502 mg) in water (5.0 mL) at 20 °C for 5 min. The crude product was purified using flash chromatography (15% Et_2O/pentane, R_f 0.40) to give 89% (221 mg) of **30** as a white solid; mp 60−64 °C (*E*/*Z*-ratio: 91/9): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, C*H*$^{\beta}$=CH$^{\alpha}$, J = 15.6 Hz, 1H), 6.99 (d, aromatic, J = 3.9 Hz, 1H), 6.97 (d, aromatic, J = 3.9 Hz, 1H), 6.11 (d, CH$^{\beta}$=C*H*$^{\alpha}$, J = 15.6 Hz, 1H) 3.77 (s, OC*H*$_3$, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0, 141.1, 136.4, 131.2, 131.1, 117.0, 116.0, 51.8; FTIR (CH_2Cl_2, cm^{-1}) 1717, 1624, 1165, 795. HRMS (EI) calcd for [$C_8H_7BrO_2S$] 245.9350, found 245.9356.

3-(5′-Methyl-2′-thiophenyl)-(*E*)-propenoic acid *tert*-butyl ester (31). 31 was obtained from a Wittig reaction between 5-methylthiophene-2-carboxaldehyde (1.0 mmol, 108 μL) and (*tert*-butoxycarbonylmethylene)triphenylphosphorane (1.5 mmol, 565 mg) in water (5.0 mL) at 20 °C for 1 h. The crude product was purified using flash chromatography (10% EtOAc/hexane, R_f 0.40) to give 97% (217 mg) of **31** as a clear oil (*E*/*Z*-ratio: 90/10): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, C*H*$^{\beta}$=CH$^{\alpha}$, J = 15.6 Hz, 1H), 7.01 (d, aromatic, J = 3.4 Hz, 1H), 6.68 (dq, aromatic, J = 3.4, 1.0 Hz, 1H), 6.02 (d, CH$^{\beta}$=C*H*$^{\alpha}$, J = 15.6 Hz, 1H), 2.48 (d, C*H*$_3$Ar, J = 1.0 Hz, 3H), 1.51 (s, O(C*H*$_3$)$_3$, 9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 166.4, 143.4, 137.8, 136.4, 131.1, 126.4, 117.6, 80.3, 28.2, 15.8; FTIR (film, cm^{-1}) 1701, 1624, 1147, 799; MS *m*/*z* 224 (M^+, 100%), 168 (M − C_4H_8, 45%), 151 (M − C_4H_9O, 35%), 135 (38%). Anal. Calcd for $C_{12}H_{16}O_2S$: C, 64.24; H, 7.19; S, 14.29. Found: C, 64.23; H, 7.36; S, 14.15.

3-(5′-Nitro-2′-thiophenyl)-(*E*)-propenoic acid *tert*-butyl ester (32). 32 was obtained from a Wittig reaction between 5-nitrothiophene-2-carboxaldehyde (1.0 mmol, 157 mg) and (*tert*-butoxycarbonylmethylene)triphenylphosphorane (1.5 mmol, 565 mg) in water (5.0 mL) at 90 °C for 1 h. The crude product was purified using flash chromatography (10% EtOAc/hexane, R_f 0.40) to give 94% (240 mg) of **32** as an orange solid; mp 87−92 °C (*E*/*Z*-ratio: 86/14): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, aromatic, J = 4.3 Hz, 1H), 7.56 (d, C*H*$^{\beta}$=CH$^{\alpha}$, J = 15.8 Hz, 1H), 7.16 (d, aromatic, J = 4.3 Hz, 1H), 6.35 (d, CH$^{\beta}$=C*H*$^{\alpha}$, J = 15.8 Hz, 1H), 1.53 (s, O(C*H*$_3$)$_3$, 9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 164.6, 145.8, 134.0, 128.9, 128.3, 124.1, 114.9, 81.5, 28.0; FTIR (CH_2Cl_2, cm^{-1}) 1707, 1631, 1265, 739. Anal. Calcd for $C_{11}H_{13}NO_4S$: C, 51.75; H, 5.13; N, 5.49; S, 12.56. Found: C, 51.75; H, 5.33; N, 5.53; S, 12.62.

3-(2′-Pyrrole)-(*E*)-propenoic acid *tert*-butyl ester (33). 33 was obtained from a Wittig reaction between pyrrole-2-carboxaldehyde (1.0 mmol, 95 mg) and (*tert*-butoxycarbonylmethylene)triphenylphosphorane (1.5 mmol, 565 mg) in water (5.0 mL) at 90 °C for 2 h. The crude product was purified using flash chromatography (10% EtOAc/hexane, R_f 0.20) to give 84% (162 mg) of **33** as a clear oil (*E*/*Z*-ratio: 99/1): ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.27 (br s, N*H*, 1H), 6.99 (m, aromatic, 1H), 6.68 (d, C*H*$^{\beta}$=CH$^{\alpha}$, J = 12.6 Hz, 1H), 6.46 (m, aromatic, 1H), 6.24 (m, aromatic, 1H), 5.45 (d, CH$^{\beta}$=C*H*$^{\alpha}$, J = 12.6 Hz, 1H), 1.52 (s, O(C*H*$_3$)$_3$, 9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 168.8, 133.8, 129.3, 122.5, 118.0, 110.0, 109.9, 80.5, 28.2; FTIR (film, cm^{-1}) 3265, 1684, 1600, 1233, 754. Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.40; H, 7.67; N, 6.98.

1-Phenyl-3-(2′-quinolinyl)-(*E*)-propenone (34).[74] **34** was obtained from a Wittig reaction between quinoline-2-carboxaldehyde (1.0 mmol, 157 mg) and (benzoylmethylene)triphenylphosphorane (1.5 mmol, 571 mg) in water (5.0 mL) at 90 °C for 2 h. The crude product was purified using flash chromatography (10% EtOAc/hexane, R_f 0.40) to give 89% (231 mg) of **34** as a orange solid; mp 114−116 °C (*E*/*Z*-ratio: 99/1) {lit.[74] mp 113−115 °C}: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (d, aromatic, J = 8.4 Hz, 1H), 8.15 (d, C*H*$^{\beta}$=CH$^{\alpha}$ "*partly hidden*", J = 15.5 Hz, 1H), 8.15−8.09 (m, aromatic, 3H), 7.94 (d, CH$^{\beta}$=C*H*$^{\alpha}$, J = 15.5 Hz, 1H), 7.81 (m, aromatic, 1H), 7.74 (m, aromatic, 1H), 7.65 (d, aromatic, J = 8.4 Hz, 1H), 7.62−7.49 (m, aromatic, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 190.6, 153.5, 148.4, 143.5, 137.9, 136.8, 133.0, 130.1, 129.9, 128.8, 128.7, 128.2, 127.6, 127.3, 127.1, 121.4; FTIR (CH_2Cl_2, cm^{-1}) 1621, 1265, 737.

3-(4′-Quinolinyl)-(*E*)-propenoic acid methyl ester (35).[75] **35** was obtained from a Wittig reaction between quinoline-4-carboxaldehyde (1.0 mmol, 157 mg) and (methoxycarbonylmethylene)-triphenylphosphorane (1.5 mmol, 502 mg) in water (5.0 mL) at 90 °C for 2 h. The crude product was purified using flash chromatography (10% EtOAc/hexane, R_f 0.40) to give 92% (196 mg) of **35** as a white solid; mp 47−49 °C (*E*/*Z*-ratio: 99/1) {lit.[75] mp 48−50 °C}: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.92 (d, aromatic, J = 4.5 Hz, 1H), 8.41 (d, C*H*$^{\beta}$=CH$^{\alpha}$, J = 15.9 Hz, 1H), 8.15 (m, aromatic, 2H), 7.78−7.74 (m, aromatic, 1H), 7.64−7.60 (m, aromatic, 1H), 7.52 (d, aromatic, J = 4.5 Hz, 1H), 6.64 (d, CH$^{\beta}$=C*H*$^{\alpha}$, J = 15.9 Hz, 1H), 3.88 (s, OC*H*$_3$, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 166.4, 150.0, 148.7, 139.9, 139.3, 130.2, 129.7, 127.3, 126.0, 124.2, 123.2, 118.1, 52.0; FTIR (CH_2Cl_2, cm^{-1}) 1720, 1644, 1176, 732.

3(3′-Pyridinyl)-(*E*)-propionic acid methyl ester (36).[72] **36** was obtained from a Wittig reaction between pyridine-3-carboxaldehyde (1.0 mmol, 94 μL) and (methoxycarbonylmethlene)triphenylphosphorane (1.5 mmol, 502 mg) in water (5.0 mL) at 20 °C for 1 h. The crude product was purified using flash chromatography (10% EtOAc/hexane, R_f 0.40) to give 88% (143 mg) of **36** as a orange solid; mp 37−41 °C (*E*/*Z*-ratio: 81/19): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.75 (d, aromatic, J = 2.2 Hz, 1H), 8.61 (dd, aromatic, J = 4.8, 1.6 Hz, 1H), 7.84 (m, aromatic, 1H), 7.68 (d, C*H*$^{\beta}$=CH$^{\alpha}$, J = 16.1 Hz, 1H), 7.32 (dd, aromatic, J = 7.9, 4.8 Hz, 1H), 6.51 (d, CH$^{\beta}$=C*H*$^{\alpha}$, J = 16.1 Hz, 1H), 3.82 (s, OC*H*$_3$, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 166.7, 151.0, 149.7, 141.1, 134.2, 130.2, 123.7, 120.1, 51.9; FTIR (CH_2Cl_2, cm^{-1}) 1718, 1641, 1172, 807.

2(*E*)-Heptenoic acid methyl ester (37).[76] **37** was obtained from a Wittig reaction between pentanal (1.0 mmol, 106 μL) and

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(methoxycarbonylmethylene)triphenylphosphorane (1.5 mmol, 502 mg) in water (5.0 mL) at 20 °C for 1 h. The crude product was purified using flash chromatography (15% Et_2O/pentane, R_f 0.80) to give 80% (114 mg) of **37** as a clear oil (*E*/*Z*-ratio: 82/18): ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.97 (dt, CH^{β}═CH$^{\alpha}$, J = 15.6, 7.1 Hz, 1H), 5.82 (dt, CH$^{\beta}$═CH^{α}, J = 15.6, 1.6 Hz, 1H), 3.72 (s, OCH_3, 3H), 2.20 (dq, methylene, J = 7.1, 7.0, 1.6 Hz, 1H), 1.48−1.40 (m, methylene, 2H), 1.39−1.30 (m, methylene, 2H), 0.91 (t, CH_3CH$_2$, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.2, 149.7, 120.8, 51.3, 31.9, 30.1, 22.2, 13.8; FTIR (film, cm^{-1}) 1728, 1658, 1174.

2(*E*)-Octenoic acid methyl ester (38).[77] **38** was obtained from a Wittig reaction between hexanal (1.0 mmol, 120 μL) and (methoxycarbonylmethylene)triphenylphosphorane (1.5 mmol, 502 mg) in water (5.0 mL) at 20 °C for 1 h. The crude product was purified using flash chromatography (15% Et_2O/pentane, R_f 0.80) to give 84% (131 mg) of **38** as a clear oil (*E*/*Z*-ratio: 81/19): ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.97 (dt, CH^{β}═CH$^{\alpha}$, J = 15.6, 7.0 Hz, 1H), 5.82 (dt, CH$^{\beta}$═CH^{α}, J = 15.6, 1.6 Hz, 1H), 3.72 (s, OCH_3, 3H), 2.19 (dq, methylene, J = 7.0, 7.0, 1.6 Hz, 2H), 1.46 (m, methylene, 2H), 1.31 (m, methylene, 4H), 0.89 (t, CH_3CH$_2$, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.2, 149.8, 120.8, 51.3, 32.2, 31.3, 27.7, 22.4, 13.9; FTIR (film, cm^{-1}) 1728, 1658, 1172; MS *m*/*z* 156 (M$^+$, 10%), 141 (M − CH_3, 2%), 125 (M − OCH_3, 10%), 113 (100%), 81 (50%).

2(*E*)-Decenoic acid methyl ester (39).[78] **39** was obtained from a Wittig reaction between octanal (1.04 mmol, 133 mg) and (methoxycarbonylmethylene)triphenylphosphorane (1.5 mmol, 502 mg) in water (5.0 mL) at 20 °C for 1 h. The crude product was purified using flash chromatography (20% EtOAc/hexane, R_f 0.60) to give 86% (164 mg) of **39** as a clear oil (*E*/*Z*-ratio: 80/20): ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.97 (dt, CH^{β}═CH$^{\alpha}$, J = 15.6, 7.0 Hz, 1H), 5.83 (dt, CH$^{\beta}$═CH^{α}, J = 15.6, 1.6 Hz, 1H), 3.72 (s, OCH_3, 3H), 2.19 (dq, methylene, J = 7.0, 7.0, 1.6 Hz, 2H), 1.50−1.40 (m, methylene, 2H), 1.32−1.22 (m, methylene, 8H), 0.88 (t, CH_3CH$_2$, J = 7.1 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 167.2, 149.8, 120.9, 51.3, 32.2, 31.8, 29.12, 29.06, 28.06, 22.6, 14.1; FTIR (film, cm^{-1}) 1728, 1658, 1171.

4-Methyl-2(*E*)-hexenoic acid *tert*-butyl ester (40).[79] **40** was obtained from a Wittig reaction between 2-methylbutyraldehyde (1.09 mmol, 94 mg) and (*tert*-butoxycarbonylmethylene)triphenylphosphorane (1.5 mmol, 565 mg) in water (5.0 mL) at 20 °C for 1 h. The crude product was purified using flash chromatography (20% EtOAc/hexane, R_f 0.40) to give 77% (153 mg) of **40** as a clear oil (*E*/*Z*-ratio: 99/1): ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.76 (dd, CH^{β}═CH$^{\alpha}$, J = 15.6, 7.7 Hz, 1H), 5.70 (dd, CH$^{\beta}$═CH^{α}, J = 15.6, 1.1 Hz, 1H), 2.19 (m, methine, 1H), 1.48 (s, OC(CH_3)$_3$, 9H), 1.45−1.35 (m, methylene, 2H), 1.03 (d, CH_3CH, J = 6.7 Hz, 3H), (t, CH_3CH$_2$, J = 7.4 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 166.3, 153.1, 121.4, 79.9, 37.9, 28.8, 28.1, 18.9, 11.6; FTIR (film, cm^{-1}) 1716, 1652, 1153, 985; MS *m*/*z* 185 (M + 1, 55%), 184 (M$^+$, 30%), 129 (95%), 111 (100%).

4-Triisopropyloxy-2(*E*),5-hexadieneoic acid methyl ester (41). 41 was obtained from a Wittig reaction between 2-triisopropyloxy-3-butenal[49] (0.515 mmol, 125 mg) and (methoxycarbonylmethylene)triphenylphosphorane (0.77 mmol, 257 mg) in water (3.0 mL) at 90 °C for 2 h. The crude product was purified using flash chromatography (5% EtOAc/hexane, R_f 0.43) to give 83% (128 mg) of **41** as a clear oil (*E*/*Z*-ratio: 88/12): ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.89 (dd, CH^{β}═CH$^{\alpha}$, J = 15.6, 4.6 Hz, 1H), 6.06 (dd, CH$^{\beta}$═CH^{α}, J = 15.6, 1.7 Hz, 1H), 5.76 (m, CH_2═CH, 1H), 5.28 (ddd, CH_2═CH, J = 17.1, 1.3, 1.3 Hz, 1H), 5.14 (ddd, CH_2═CH, J = 10.3, 1.3, 1.3 Hz, 1H), 4.87 (m, CHOSi, 1H), 3.74 (s, OCH_3, 3H), 1.13−1.04 (br m, Si(*i*-Pr)$_3$, 21H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 167.1, 149.8, 138.6, 119.2, 115.3, 73.4, 51.6, 18.0, 12.3; FTIR (CH_2Cl_2, cm^{-1}) 2946, 1731, 1165, 883; MS *m*/*z* 298 (M, 0.5%), 255 (M − ^{i}Pr, 100%), 145 (43%).

2(*E*)-Butenedioic acid mono-*tert*-butyl ester (42).[80] **42** was obtained from a Wittig reaction between glyoxylic acid, 50 wt % solution in water (1.36 mmol, 201 mg) and (*tert*-butoxycarbonylmethylene)triphenylphosphorane (1.36 mmol, 512 mg) in water (5.0 mL) at 20 °C for 30 min. The crude product (est. 75%, 175 mg; *E*/*Z*-ratio: ∼70:30) was purified through a silica gel plug (25% EtOAc/hexane, R_f 0.20) to give 30−50% (117 mg) of fumaric acid mono-*tert*-butyl ester (***E*-42**) as a white solid; mp 65−68 °C (*E*/*Z*-ratio: 99/1): ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.86 (d, olefinic, J = 15.8 Hz, 1H), 6.76 (d, olefinic, J = 15.8 Hz, 1H), 1.52 (s, C(CH_3)$_3$, 9H); ^{1}H NMR (DMSO-d_6) δ 13.1 (b, CO_2H, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 169.6, 163.9, 137.7, 131.6, 82.3, 28.0; FTIR (CH_2Cl_2, cm^{-1}) 2983, 1707, 1154, 908; MS *m*/*z* 172 (M$^+$, 28%), 57 (C_4H_9, 100%).

3-(4′-Bromo-2′-thiophenyl)-(*E*)-propenoic acid methyl ester (44). 44 was obtained from a Wittig reaction between 4-bromothiophene-2-carboxaldehyde (1.1 mmol, 210 mg) and (methoxycarbonylmethylene)triphenylphosphorane (1.5 mmol, 502 mg) in water (5.0 mL) at 80 °C for 2 h. The crude product was purified using flash chromatography (20% EtOAc/hexane, R_f 0.40) to give 99% (245 mg) of **44** as a yellow solid; mp 64−67 °C (*E*/*Z*-ratio: 96/4): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, CH^{β}═CH$^{\alpha}$, J = 15.8 Hz, 1H), 7.25 (s, aromatic, 1H), 7.15 (s, aromatic, 1H), 6.24 (d, CH$^{\beta}$═CH^{α}, J = 15.8 Hz, 1H), 3.79 (s, OCH_3, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 166.7, 140.2, 135.8, 132.3, 125.1, 117.9, 110.9, 51.8; FTIR (CH_2Cl_2, cm^{-1}) 1713, 1632, 1265, 739. Anal. Calcd for $C_8H_7BrO_2S$: C, 38.88; H, 2.86; S, 12.94. Found: C, 38.76; H, 3.11; S, 12.64.

3-(4′-Dimethylaminophenyl)-(*E*)-propenoic acid ethyl ester (48).[81] **48** was obtained from a Wittig reaction between 4-dimethylaminobenzaldehyde (1.0 mmol, 149 mg), triphenylphosphine (1.5 mmol, 393 mg), and ethyl bromoacetate (1.8 mmol, 200 μL) in saturated $NaHCO_3$ (5 mL) at 20 °C for 2 h. The crude product was purified using flash chromatography (20% EtOAc/hexane, R_f 0.30) to give 32% (70.1 mg) of **48** as a yellow solid; mp 74−76 °C (*E*/*Z*-ratio: 99/1): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, CH^{β}═CH$^{\alpha}$, J = 15.9 Hz, 1H), 7.42 (m, aromatic, 2H), 6.67 (m, aromatic, 2H), 6.22 (d, CH$^{\beta}$═CH^{α}, J = 15.9 Hz, 1H), 4.23 (q, OCH_2, J = 7.2 Hz, 2H), 3.01 (s, N(CH_3)$_2$, 6H), 1.32 (t, CH_3CH$_2$, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.9, 151.8, 145.1, 129.7, 122.4, 112.7, 111.9, 60.1, 40.2, 14.4; FTIR (CH_2Cl_2, cm^{-1}) 1701, 1601, 1265, 738; MS *m*/*z* 219 (M$^+$, 100%), 174 (M − OEt, 38%), 146 (M − CO_2Et, 25%).

3-(4′-Chlorophenyl)-(*E*)-propenoic acid ethyl ester (49).[81] **49** was obtained from a Wittig reaction between 4-chlorobenzaldehyde (1.0 mmol, 141 mg), triphenylphosphine (1.5 mmol, 393 mg), and ethyl bromoacetate (1.8 mmol, 200 μL) in saturated $NaHCO_3$ (5 mL) at 20 °C for 2 h. The crude product was purified using flash chromatography (20% EtOAc/hexane, R_f 0.40) to give 99% (208 mg) of **49** as a light yellow oil (*E*/*Z*-ratio: 89/11): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, CH^{β}═CH$^{\alpha}$, J = 16.0 Hz, 1H), 7.45 (m, aromatic, 2H), 7.36 (m, aromatic, 2H), 6.40 (d, CH$^{\beta}$═CH^{α}, J = 16.0 Hz, 1H), 4.27 (q, OCH_2, J = 7.1 Hz, 2H), 1.34 (t, CH_3CH$_2$, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7, 143.1, 136.1, 133.0, 129.20, 129.18, 118.9, 60.6, 14.3; FTIR (film, cm^{-1}) 1709, 1640, 1265, 908; MS *m*/*z* 211 (M + 1, 100%), 165 (M − OEt, 48%), 102 (25%).

3-(4′-Chlorophenyl)-(*E*)-propenoic acid benzyl ester (50). 50 was obtained from a Wittig reaction between 4-chlorobenzaldehyde (1.0 mmol, 141 mg), triphenylphosphine (1.6 mmol, 420 mg), and

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benzyl bromoacetate (1.4 mmol, 221 μL) in saturated $NaHCO_3$ (5 mL) at 20 °C for 2 h. The crude product was purified using flash chromatography (10% EtOAc/hexane, R_f 0.34) to give 84% (228 mg) of **50** as a white solid; mp 65−68 °C (*E*/*Z*-ratio: 92/8): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, C*H*$^{\beta}$=CH$^{\alpha}$, *J* = 16.0 Hz, 1H), 7.46−7.43 (m, aromatic, 2H), 7.42−7.32 (m, aromatic, 6H), 6.45 (d, CH$^{\beta}$=C*H*$^{\alpha}$, *J* = 16.0 Hz, 1H), 5.25 (s, OC*H*$_2$Ph, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 143.7, 136.3, 136.0, 132.9, 131.1, 129.3, 129.2, 128.6, 128.3, 118.5, 66.5; FTIR (CH_2Cl_2, cm^{-1}) 1715, 1638, 1265, 739; MS *m*/*z* 274 (M + 2, 10%), 273 (M + 1, 5%), 272 (M$^+$, 20%), 237 (35%), 226 (85%), 165 (M − C_7H_7O, 100%), 91 (60%). HRMS (EI, DCI/NH_3) calcd for $[C_{16}H_{17}NO_2Cl]^+$ (MNH^+) 290.0948, found 290.0946.

3-(4′-Methoxyphenyl)-(*E*)-propenoic acid ethyl ester (51).[81] **51** was obtained from a Wittig reaction between 4-methoxybenzaldehyde (1.0 mmol, 122 μL), triphenylphosphine (1.5 mmol, 393 mg), and ethyl bromoacetate (1.8 mmol, 200 μL) in saturated $NaHCO_3$ (5 mL) at 20 °C for 2 h. The crude product was purified using flash chromatography (10% EtOAc/hexane, R_f 0.20) to give 94% (194 mg) of **51** as a colorless oil (*E*/*Z*-ratio: 93/7): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, C*H*$^{\beta}$=CH$^{\alpha}$, *J* = 16.0 Hz, 1H), 7.47 (m, aromatic, 2H), 6.90 (m, aromatic, 2H), 6.30 (d, CH$^{\beta}$=C*H*$^{\alpha}$, *J* = 16.0 Hz, 1H), 4.25 (q, OC*H*$_2$, *J* = 7.2 Hz, 2H), 3.84 (s, OMe, 3H), 1.33 (t, C*H*$_3$CH$_2$, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.3, 161.4, 144.3, 129.7, 127.3, 115.8, 114.3, 60.3, 55.4, 14.4; FTIR (film, cm^{-1}) 1716, 1635, 1248, 829; MS *m*/*z* 206 (M$^+$, 100%), 161 (M − OEt, 25%).

3-(4′-Methoxyphenyl)-(*E*)-propenoic acid benzyl ester (52).[82] **52** was obtained from a Wittig reaction between 3-benzyloxybenzaldehyde (1.0 mmol, 121 μL), triphenylphosphine (1.6 mmol, 420 mg), and benzyl bromoacetate (1.4 mmol, 221 μL) in saturated $NaHCO_3$ (5 mL) at 20 °C for 2 h. The crude product was purified using flash chromatography (20% EtOAc/hexane, R_f 0.37) to give 86% (230 mg) of **52** as a white solid; mp 45−47 °C (*E*/*Z*-ratio: 91/9): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, C*H*$^{\beta}$=CH$^{\alpha}$, *J* = 15.9 Hz, 1H), 7.48−7.44 (m, aromatic, 2H), 7.43−7.30 (m, aromatic, 5H), 6.89 (m, aromatic, 2H), 6.35 (d, CH$^{\beta}$=C*H*$^{\alpha}$, *J* = 15.9 Hz, 1H), 5.24 (s, OC*H*$_2$Ph, 2H), 3.82 (s, OC*H*$_3$, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.1, 161.5, 144.8, 136.3, 129.8, 128.6, 128.24, 128.19, 127.2, 115.4, 114.4, 66.2, 55.4; FTIR (CH_2Cl_2, cm^{-1}) 1709, 1635, 1604, 1265, 908, 734; MS *m*/*z* 268 (M$^+$, 100%), 223 (73%), 161 (M−PhC*H*$_2$O, 74%), 134 (80%), 91 (95%).

3-(3′-Benzyloxyphenyl)-(*E*)-propenoic acid ethyl ester (53).[83] **53** was obtained from a Wittig reaction between 3-benzyloxybenzaldehyde (1.0 mmol, 212 mg), triphenylphosphine (1.5 mmol, 393 mg), and ethyl bromoacetate (1.8 mmol, 200 μL) in saturated $NaHCO_3$ (5 mL) at 20 °C for 2 h. The crude product was purified using flash chromatography (10% EtOAc/hexane, R_f 0.30) to give 99% (280 mg) of **53** as a white solid; mp 39−40 °C (*E*/*Z*-ratio: 92/8): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, C*H*$^{\beta}$=CH$^{\alpha}$, *J* = 16.0 Hz, 1H), 7.45−7.36 (2m, aromatic, 2H each), 7.35−7.25 (m, aromatic, 2H), 7.12 (m, aromatic, 2H), 6.99 (m, aromatic, 1H), 6.40 (d, CH$^{\beta}$=C*H*$^{\alpha}$, *J* = 16.0 Hz, 1H), 5.08 (s, OC*H*$_2$Ph, 2H), 4.26 (q, OC*H*$_2$CH$_3$, *J* = 7.2 Hz, 2H), 1.33 (t, C*H*$_3$CH$_2$, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.9, 159.1, 144.4, 136.7, 135.9, 130.0, 128.6, 128.1, 127.5, 121.0, 118.7, 117.0, 114.0, 70.1, 60.5, 14.3; FTIR (CH_2Cl_2, cm^{-1}) 1708, 1639, 1266, 742; MS *m*/*z* 282 (M$^+$, 86%), 237 (M − OEt, 23%), 208 (45%), 191 (M − C_7H_7, 100%), 91 (28%).

3-(3′-Benzyloxyphenyl)-(*E*)-propenoic acid *tert*-butyl ester (54). 54 was obtained from a Wittig reaction between 3-benzyloxybenzaldehyde (1.0 mmol, 217 mg), triphenylphosphine (1.4 mmol, 366 mg), and *tert*-butyl bromoacetate (1.6 mmol, 240 μL) in saturated $NaHCO_3$ (5 mL) at 20 °C for 3 h. The crude product was purified using flash chromatography (10% EtOAc/hexane, R_f 0.25) to give 96% (297 mg) of **54** as a colorless oil (*E*/*Z*-ratio: 93/7): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, C*H*$^{\beta}$=CH$^{\alpha}$, *J* = 16.0 Hz, 1H), 7.45−7.36 (2m, aromatic, 2H each), 7.35−7.24 (2m, aromatic, 1H each), 7.12−7.09 (m, aromatic, 2H), 6.98 (m, aromatic, 1H), 6.34 (d, CH$^{\beta}$=C*H*$^{\alpha}$, *J* = 16.0 Hz, 1H), 5.08 (s, OC*H*$_2$Ph, 2H), 1.53 (s, C(C*H*$_3$)$_3$, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.2, 159.1, 143.4, 136.7, 136.2, 129.8, 128.6, 128.1, 127.5, 120.9, 120.6, 116.7, 113.9, 80.5, 70.1, 28.2; FTIR (film, cm^{-1}) 1703, 1422, 1264, 738; MS *m*/*z* 310 (M$^+$, 5%), 254 (M, 85%), 237 (M − O*t*Bu, 82%), 91 (C_7H_7, 100%). Anal. Calcd for $C_{20}H_{22}O_3$: C, 77.39; H, 7.14. Found: C, 77.23; H, 6.85.

3-(2′,5′-Dimethylphenyl)-(*E*)-propenoic acid ethyl ester (55).[84] **55** was obtained from a Wittig reaction between 2,5-dimethylbenzaldehyde (1.0 mmol, 142 μL), triphenylphosphine (1.5 mmol, 393 mg), and ethyl bromoacetate (1.8 mmol, 200 μL) in saturated $NaHCO_3$ (5 mL) at 20 °C for 2 h. The crude product was purified using flash chromatography (10% EtOAc/hexane, R_f 0.25) to give 97% (194 mg) of **55** as a light yellow oil (*E*/*Z*-ratio: 92/8): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, C*H*$^{\beta}$=CH$^{\alpha}$, *J* = 15.9 Hz, 1H), 7.36 (s, aromatic, 1H), 7.08 (2d, aromatic, "partly overlap", 2H), 6.34 (d, CH$^{\beta}$=C*H*$^{\alpha}$, *J* = 15.9 Hz, 1H), 4.26 (q, OC*H*$_2$, *J* = 7.1 Hz, 2H), 2.39, 2.32 (2s, Ar−C*H*$_3$, 3H each), 1.34 (t, C*H*$_3$CH$_2$, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.1, 142.4, 135.7, 134.6, 133.2, 130.8, 130.7, 127.0, 119.0, 60.4, 20.9, 19.3, 14.3; FTIR (film, cm^{-1}) 1706, 1635, 1265, 908; MS *m*/*z* 205 (M + 1, 100%), 189 (M − CH_3, 5%), 159 (M − OEt, 15%), 130 (18%).

3-(2′-Benzyloxyphenyl)-(*E*)-propenoic acid *tert*-butyl ester (56). 56 was obtained from a Wittig reaction between 2-benzyloxybenzaldehyde (1.0 mmol, 217 mg), triphenylphosphine (1.4 mmol, 366 mg), and *tert*-butyl bromoacetate (1.6 mmol, 240 μL) in saturated $NaHCO_3$ (5 mL) at 20 °C for 3 h. The crude product was purified using flash chromatography (10% EtOAc/hexane, R_f 0.20) to give 92% (285 mg) of **56** as a colorless oil (*E*/*Z*-ratio: 72/28): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, C*H*$^{\beta}$=CH$^{\alpha}$, *J* = 16.1 Hz, 1H), 7.55−7.51 (m, aromatic, 1H), 7.46−7.35 (m, aromatic, 4H), 7.34−7.23 (m, aromatic, 2H), 6.97−6.90 (m, aromatic, 2H), 6.45 (d, CH$^{\beta}$=C*H*$^{\alpha}$, *J* = 16.1 Hz, 1H), 5.15 (s, OC*H*$_2$Ph, 2H), 1.52 (s, C(C*H*$_3$)$_3$, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7, 157.2, 138.7, 136.7, 131.1, 129.9, 128.6, 128.5, 128.0, 127.1, 121.0, 120.7, 112.8, 80.1, 70.4, 28.2; FTIR (film, cm^{-1}) 1702, 1632, 1422, 1265, 738; MS *m*/*z* 311 (M + 1, 5%), 255 (100%). Anal. Calcd for $C_{20}H_{22}O_3$: C, 77.39; H, 7.14. Found: C, 77.04; H, 6.89.

3-(2′-Methylphenyl)-(*E*)-propenoic acid benzyl ester (57). 57 was obtained from a Wittig reaction between 2-methylbenzaldehyde (1.0 mmol, 120 μL), triphenylphosphine (1.2 mmol, 319 mg), and benzyl bromoacetate (1.3 mmol, 215 μL) in saturated $NaHCO_3$ (5 mL) at 20 °C for 3 h. The crude product was purified using flash chromatography (10% Et_2O/pentane, R_f 0.70) to give 90% (227 mg) of **57** as a colorless oil (*E*/*Z*-ratio: 94/6): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, C*H*$^{\beta}$=CH$^{\alpha}$, *J* = 15.9 Hz, 1H), 7.54 (m, aromatic, 1H), 7.44−7.31 (m, aromatic, 5H), 7.31−7.25 (m, aromatic, 1H), 7.22−7.18 (m, aromatic, 2H), 6.41 (d, CH$^{\beta}$=C*H*$^{\alpha}$, *J* = 15.9 Hz, 1H), 5.26 (s, OC*H*$_2$Ph, 2H), 2.43 (s, C*H*$_3$Ph, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.8, 142.9, 137.7, 136.1, 133.3, 130.8, 130.0, 128.6, 128.22, 128.20, 126.4, 126.3, 118.9, 66.3, 19.7; FTIR (film, cm^{-1}) 1709, 1634, 1313, 1168, 723; MS *m*/*z* 252 (M$^+$, 5%), 206 (100%), 161 (M − C_7H_7, 87%), 145 (M − C_7H_7O, 95%), 91 (12%). Anal. Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 80.58; H, 6.23.

3-(Pentafluorophenyl)-(*E*)-propenoic acid benzyl ester (58). 58 was obtained from a Wittig reaction between pentafluorobenzaldehyde (1.0 mmol, 123 μL), triphenylphosphine (1.6 mmol, 420 mg), and benzyl bromoacetate (1.4 mmol, 221 μL) in saturated $NaHCO_3$ (5 mL) at 20 °C for 2 h. The crude product was purified using flash chromatography (10% EtOAc/hexane, R_f 0.30) to give 82% (269 mg) of **58** as a white solid; mp 62−64 °C (*E*/*Z*-ratio:

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98/2): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, CH^{β}=CH$^{\alpha}$, J = 16.5 Hz, 1H), 7.43−7.32 (m, aromatic, 5H), 6.79 (d, CH$^{\beta}$=CH^{α}, J = 16.5 Hz, 1H), 5.27 (s, OCH_2Ph, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.8, 145.7, 141.8, 137.8, 135.6, 132.2, 128.7, 128.5, 128.4, 126.0, 109.9, 67.0; ^{19}F NMR (188 MHz, $CDCl_3$) δ −140.6, −152.2, −162.7; FTIR (CH_2Cl_2, cm^{-1}) 1720, 1500, 1265, 739; MS m/z 328 (M$^+$, 12%), 283 (65%), 221 (M − PhCH$_2$O, 70%), 91 (100%). Anal. Calcd for $C_{16}H_9F_5O_2$: C, 58.55; H, 2.76. Found: C, 58.26; H, 2.85.

3-(Pentafluorophenyl)-(*E*)-propenoic acid *tert*-butyl ester (59). 59 was obtained from a Wittig reaction between pentafluorobenzaldehyde (1.0 mmol, 196 mg), triphenylphosphine (1.4 mmol, 366 mg), and *tert*-butyl bromoacetate (1.6 mmol, 240 μL) in saturated $NaHCO_3$ (5 mL) at 20 °C for 40 min. The crude product was purified using flash chromatography (10% EtOAc/hexane, R_f 0.40) to give 84% (194 mg) of **59** as a white solid; mp 37−38 °C (*E*/*Z*-ratio: 98/2): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, CH^{β}=CH$^{\alpha}$, J = 16.5 Hz, 1H), 6.66 (d, CH$^{\beta}$=CH^{α}, J = 16.5 Hz, 1H), 1.54 (s, C(CH_3)$_3$, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.3, 145.6, 141.6, 137.9, 128.4, 127.1, 110.2, 81.6, 28.1; FTIR (CH_2Cl_2, cm^{-1}) 1709, 1500, 1265, 739; MS m/z 295 (M + 1, 78%), 239 (100%). HRMS (EI) calcd for $[C_{13}H_{11}O_2F_5]^+$ 294.0679, found 294.0668.

3-(2′-Nitrophenyl)-(*E*)-propenoic acid *tert*-butyl ester (60). 60 was obtained from a Wittig reaction between 2-nitrobenzaldehyde (1.0 mmol, 156 mg), triphenylphosphine (1.4 mmol, 366 mg), and *tert*-butyl bromoacetate (1.6 mmol, 240 μL) in saturated $NaHCO_3$ (5 mL) at 20 °C for 1.5 h. The crude product was purified using flash chromatography (10% EtOAc/hexane, R_f 0.20) to give 99% (194 mg) of **60** as a yellow solid; mp 60−62 °C (*E*/*Z*-ratio: 85/15): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, CH^{β}=CH$^{\alpha}$, J = 15.7 Hz, 1H), 8.01 (m, aromatic, "partly hidden", 1H), 7.65−7.62 (m, aromatic, 2H), 7.54−7.50 (m, aromatic, 1H), 6.30 (d, CH$^{\beta}$=CH^{α}, J = 15.7 Hz, 1H), 1.54 (s, C(CH_3)$_3$, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 148.4, 138.7, 133.4, 130.8, 130.0, 129.1, 125.3, 124.8, 81.2, 28.2; FTIR (CH_2Cl_2, cm^{-1}) 1710, 1638, 1152, 976; MS m/z 249 (M$^+$, 60%), 232 (50%), 221 (53%), 120 (53%), 102 (100%), 89 (78%). Anal. Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.89; H, 5.78; N, 5.78.

3(3′-Pyridinyl)-(*E*)-propionic acid ethyl ester (61).[85] **61** was obtained from a Wittig reaction between 3-pyridinecarboxaldehyde (1.0 mmol, 96 μL), triphenylphosphine (1.5 mmol, 393 mg), and ethyl bromoacetate (1.8 mmol, 200 μL) in saturated $NaHCO_3$ (5 mL) at 20 °C for 1 h. The crude product was purified using flash chromatography (20% EtOAc/hexane, R_f 0.16) to give 81% (143 mg) of **61** as a colorless oil (*E*/*Z*-ratio: 87/13): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.75 (br s, aromatic, 1H), (br m, aromatic, 1H), 7.83 (dt, aromatic, J = 7.9, 1.8 Hz, 1H), 7.67 (d, CH^{β}=CH$^{\alpha}$, J = 16.1 Hz, 1H), 7.33 (dd, aromatic, J = 7.9, 4.9 Hz, 1H), 6.51 (d, CH$^{\beta}$=CH^{α}, J = 16.1 Hz, 1H), 4.29 (q, OCH_2CH$_3$, J = 7.2 Hz, 2H), 1.35 (t, CH_3CH$_2$, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.3, 151.0, 149.7, 140.9, 134.2, 130.3, 123.7, 120.6, 60.8, 14.3; FTIR (film, cm^{-1}) 1712, 1421, 1265, 735; MS m/z 178 (M + 1, 100%), 132 (M − OEt, 47%), 104 (28%).

3-(4′-Hydroxy)-(*E*)-propenoic acid benzyl ester (62).[86] **62** was obtained from a Wittig reaction between 4-hydroxybenzaldehyde (1.0 mmol, 122 mg), triphenylphosphine (1.6 mmol, 420 mg), and benzyl bromoacetate (1.4 mmol, 221 μL) in saturated $NaHCO_3$ (5 mL) at 20 °C for 2 h. The crude product was purified using flash chromatography (33% EtOAc/hexane, R_f 0.37) to give 64% (163 mg) of **62** as a white solid; mp 87−89 °C (*E*/*Z*-ratio: 94/6) {lit.[86] mp 90−92 °C}: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, CH^{β}=CH$^{\alpha}$, J = 16.0 Hz, 1H), 7.43−7.31 (m, aromatic, 7H), 6.83 (m, aromatic, 2H), 6.34 (d, CH$^{\beta}$=CH^{α}, J = 16.0 Hz, 1H), 5.54 (br s, *H*OPh, 1H), 5.25 (s, OCH_2Ph, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.4, 157.8, 145.0, 136.2, 130.0, 128.6, 128.25, 128.24, 127.2, 115.9, 115.3, 66.3; FTIR (CH_2Cl_2, cm^{-1}) 3363, 1708, 1606, 1265, 738.

3-(5′-Methyl-2′-thiophenyl)-(*E*)-propenoic acid ethyl ester (63).[87] **63** was obtained from a Wittig reaction between 5-methyl-2-thiophenecarboxaldehyde (1.0 mmol, 129 mg), triphenylphosphine (1.5 mmol, 393 mg), and ethyl bromoacetate (1.8 mmol, 200 μL) in saturated $NaHCO_3$ (5 mL) at 20 °C for 1 h. The crude product was purified using flash chromatography (10% EtOAc/hexane, R_f 0.40) to give 99% (194 mg) of **63** as a light yellow oil (*E*/*Z*-ratio: 93/7): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, CH^{β}=CH$^{\alpha}$, J = 15.6 Hz, 1H), 7.04 (d, aromatic, J = 3.5 Hz, 1H), 6.70 (dq, aromatic, J = 3.5, 0.9 Hz, 1H), 6.10 (d, CH$^{\beta}$=CH^{α}, J = 15.6 Hz, 1H), 4.23 (q, OCH_2CH$_3$, J = 7.2 Hz, 2H), 2.49 (d, CH_3Ar, J = 0.9 Hz, 3H), 1.32 (t, CH_3CH$_2$, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.1, 143.9, 137.6, 137.4, 131.5, 126.5, 115.6, 60.3, 15.8, 14.4; FTIR (film, cm^{-1}) 1702, 1624, 1422, 1265, 738; MS m/z 197 (M + 1, 62%), 151 (M − OEt, 100%).

3-(5′-Bromo-2′-thiophenyl)-(*E*)-propenoic acid *tert*-butyl ester (64). 64 was obtained from a Wittig reaction between 5-bromo-2-thiophenecarboxaldehyde (1.0 mmol, 192 mg), triphenylphosphine (1.4 mmol, 366 mg), and *tert*-butyl bromoacetate (1.6 mmol, 240 μL) in saturated $NaHCO_3$ (5 mL) at 20 °C for 1.5 h. The crude product was purified using flash chromatography (5% Et_2O/pentane, R_f 0.50) to give 99% (286 mg) of **64** as a light yellow oil (*E*/*Z*-ratio: 91/9): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, CH^{β}=CH$^{\alpha}$, J = 15.7 Hz, 1H), 6.99 (d, aromatic, J = 3.9 Hz, 1H), 6.95 (d, aromatic, J = 3.9 Hz, 1H), 6.06 (d, CH$^{\beta}$=CH^{α}, J = 15.7 Hz, 1H), 1.51 (s, C(CH_3)$_3$, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.8, 141.4, 135.2, 131.0, 130.7, 119.5, 115.3, 80.8, 28.2; FTIR (film, cm^{-1}) 1701, 1626, 1264, 739; MS m/z 290 (M + 2, 42%), 288 (M$^+$, 52%), 233 (100%). HRMS (EI, DCI/NH_3) calcd for $[C_{11}H_{17}NO_2SBr]^+$ (MNH$^+$) 306.0163, found 306.0156.

3-(4′-Bromo-2′-thiophenyl)-(*E*)-propenoic acid ethyl ester (65).[87] **65** was obtained from a Wittig reaction between 4-bromo-2-thiophenecarboxaldehyde (1.0 mmol, 192 mg), triphenylphosphine (1.5 mmol, 393 mg), and ethyl bromoacetate (1.8 mmol, 200 μL) in saturated $NaHCO_3$ (5 mL) at 20 °C for 1 h. The crude product was purified using flash chromatography (20% EtOAc/hexane, R_f 0.30) to give 98% (255 mg) of **65** as a white solid; mp 62−63 °C (*E*/*Z*-ratio: 88/12): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, CH^{β}=CH$^{\alpha}$, J = 15.8 Hz, 1H), 7.25, 7.15 (br s, aromatic, 1H each), 6.24 (d, CH$^{\beta}$=CH^{α}, J = 15.8 Hz, 1H), 4.25 (q, OCH_2CH$_3$, J = 7.2 Hz, 2H), 1.32 (t, CH_3CH$_2$, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.3, 140.4, 135.6, 132.3, 125.1, 118.5, 110.9, 60.7, 14.3; FTIR (CH_2Cl_2, cm^{-1}) 1708, 1631, 1265, 908, 734; MS m/z 261 (M$^+$, 60%), 260 (M − 1, 100%), 215 (M − HOEt, 60%). HRMS (EI, DCI/NH_3) calcd for $[C_9H_{10}SO_2Br]^+$ (MH$^+$) 260.9585, found 260.9576.

3-(4′-Bromo-2′-thiophenyl)-(*E*)-propenoic acid *tert*-butyl ester (66). 66 was obtained from a Wittig reaction between 4-bromo-2-thiophenecarboxaldehyde (1.0 mmol, 192 mg), triphenylphosphine (1.4 mmol, 366 mg), and *tert*-butyl bromoacetate (1.6 mmol, 240 μL) in saturated $NaHCO_3$ (5 mL) at 20 °C for 1.5 h. The crude product was purified using flash chromatography (5% Et_2O/pentane, R_f 0.80) to give 99% (286 mg) of **66** as a colorless oil (*E*/*Z*-ratio: 99/1): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, CH^{β}=CH$^{\alpha}$, J = 15.8 Hz, 1H), 7.22, 7.12 (br s, aromatic, 1H each), 6.18 (d, CH$^{\beta}$=CH^{α}, J = 15.8 Hz, 1H), 1.52 (s, C(CH_3)$_3$, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.6, 140.6, 134.6, 131.9, 124.7, 120.5, 110.8, 80.9, 28.2; FTIR (film, cm^{-1}) 1703, 1629, 1265, 739; MS m/z 290 (M + 2, 24%), 288 (M$^+$, 32%), 233 (44%), 217 (100%).

3-(2′-Thiophenyl)-(*E*)-propenoic acid *tert*-butyl ester (67).[88] **67** was obtained from a Wittig reaction between 2-thiophenecarboxaldehyde (1.0 mmol, 100 μL), triphenylphosphine (1.4 mmol, 366 mg), and *tert*-butyl bromoacetate (1.6 mmol, 240 μL) in

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saturated $NaHCO_3$ (5 mL) at 20 °C for 1.5 h. The crude product was purified using flash chromatography (20% Et_2O/pentane, R_f 0.50) to give 99% (208 mg) of **67** as a light yellow oil (*E/Z*-ratio: 92/8): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, C*H*$^{\beta}$=CH$^{\alpha}$, J = 15.6 Hz, 1H), 7.34 (d, aromatic, J = 5.0 Hz, 1H), 7.21 (d, aromatic, J = 3.7 Hz, 1H), 7.03 (dd, aromatic, J = 5.0, 3.7 Hz, 1H), 6.17 (d, CH$^{\beta}$=C*H*$^{\alpha}$, J = 15.6 Hz, 1H), 1.52 (s, C(C*H*$_3$)$_3$, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.1, 139.8, 136.0, 130.4, 127.97, 127.93, 119.1, 80.5, 28.2; FTIR (film, cm^{-1}) 1701, 1627, 1392, 1150, 971, 853; MS *m*/*z* 210 (M$^+$, 28%), 155 (75%), 137 (M − ^{t}BuO, 100%), 121 (88%).

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Supporting Information Available: General and chemical information plus copies of relevant ^{1}H and ^{13}C NMR spectra of compounds **2**−**42**, **44**, **46**−**67**. This material is available free of charge via the Internet at http://pubs.acs.org.

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