Selectivity Reversal during Thia-Michael Additions Using Tetrabutylammonium Hydroxide: Operationally Simple and Extremely High Turnover

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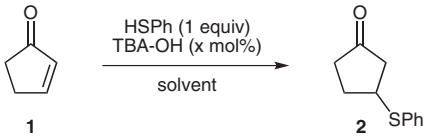
Abstract: The use of tetrabutylammonium hydroxide as a novel and exceedingly efficient thia-Michael addition catalyst is herein described. This extremely simple methodology allows for the conjugate addition of a wide variety of mercaptan nucleophiles, and functions remarkably well with a very wide range of both classical and non-classical Michael acceptors. Contradistinctive to current literature reports, the use of this catalyst more efficiently promotes the addition of more basic thiols. This methodology is especially attractive and operationally simple, as it generally proceeds with only 1 mol% catalytic loading and without excess reagent, and the produced products typically require no purification.

Key words: thia-Michael reaction, conjugate addition, catalysis, green chemistry, high turnover number, selectivity reversal

The Michael addition of nucleophiles to α,β-unsaturated systems is one of the most important bond forming processes in synthetic organic chemistry. Of special interest are the sulfur variants of this reaction, historically referred to as the thia-Michael reaction, which provide access to β-thiocarbonyl compounds.[1] These highly interesting compounds are of great importance, as they often possess biological and pharmacological activity,[2] and can also be used as auxiliaries in further synthetic manipulation.[3] Typically, thia-Michael reactions are promoted by: certain bases;[1a,2c,4] the fluoride ion;[5] functionalized clays[6] and silica gel,[4b,7] iodine,[8] lanthanum salts;[9] Brønsted–Lowry acids;[10] or metals such as copper,[11] cadmium,[12] bismuth,[13] ruthenium,[14] or vanadium.[15] (The direct addition of thiolate anions has also been described.[16]) The use of these catalysts often requires harsh conditions, elevated temperatures, prolonged reaction times, or special precautions such as the employment of inert atmosphere techniques, tedious purification methods, or pH-altered media. Furthermore, superstoichiometric quantities of catalysts or reagents are frequently required for full promotion. For these reasons, new and improved catalysts for this reaction are still being sought. In designing such catalysts, special consideration should be given to the cost and atom-economy of potential promoters.[17] Additionally, the choice of solvent and catalyst should be made with the consideration of potential environmental impact in mind;[18] very high catalytic turnover is especially critical when making considerations for scale-up to an industrial level. In certain cases, the use of water as a solvent has been shown to catalyze thia-Michael additions efficiently.[19] While these reports have offered an excellent advancement in the promotion of this reaction, the requisite use of silica gel chromatography for these methods significantly retracts from their attraction. As such, further promotional methods that provide pure products directly and expand the generality of this methodology away from explicit carbonyl functionalities are highly desirable.

We began our studies by considering the model reaction of cyclopent-2-en-1-one (**1**) with one equivalent of benzenethiol (pK_a ≈ 6.6) in alcoholic solvents. Without the aid of an additional catalyst, only trace amounts of thia-Michael product **2** were observable by TLC analysis after two hours (Table 1, entry 1). An observation we made during work on an unrelated project involving mostly P–C bond formation indicated to us that an aqueous solution of tetrabutylammonium hydroxide (TBA-OH) in an alcoholic solvent could potentially serve as an effective catalyst for this reaction.

Table 1 Optimization of Reaction Parameters



1 2

Entry	Solvent	TBA-OH (mol%)	Time (min)	Yield (%)
1	ROH	–	120	trace
2	MeOH	10	<1	>99
3	EtOH	10	<1	>99
4	EtOH	5	1	>99
5	EtOH	1	2	>99
6	EtOH	0.1	5	>99
7	EtOH	0.01	10	>99

Testing this theory, we found that the addition of 10 mol% of an aqueous solution of tetrabutylammonium hydroxide was found to offer complete formation of the addition product almost instantaneously. With this in mind, we performed an optimization study to improve the efficacy of this novel catalyst (Table 1). We noted that, under catalytic conditions, the reaction proceeded readily in alcoholic solvents such as methanol and ethanol (entries 2 and

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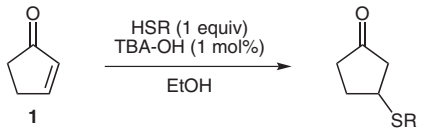
3), but opted for the use of the latter, as it is a preferred solvent from an environmental standpoint. Remarkably, we found that even 0.01 mol% (10,000 TON) of tetrabutylammonium hydroxide catalyst could effectively promote the reaction (entry 7). Tetrabutylammonium hydroxide is not reported to possess any RCRA-classified hazards,[20] it is a readily available and inexpensive reagent,[21] its use does not require special techniques or considerations, and it can be readily removed due to its insolubility in diethyl ether.

Table 2 Application of Thia-Michael Catalysis Conditions to a Variety of Mercaptans



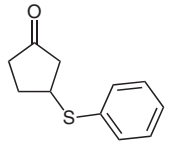
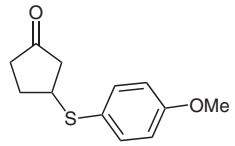
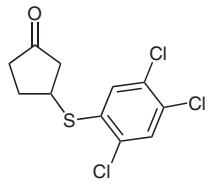
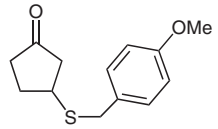
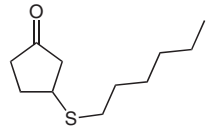
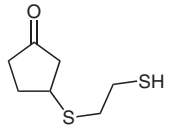
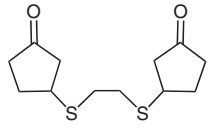
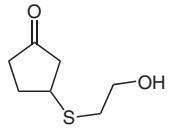
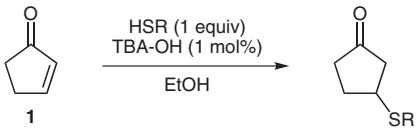
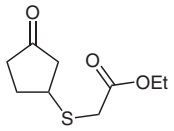
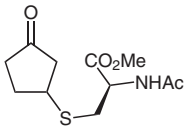
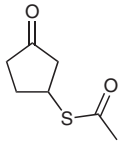
Entry	Product		Time	Yield[a] (%)
1		**2**	2 min	>99
2		**3**	1 min	>99
3		**4**	30 min	73
4		**5**	2 h	90
5		**6**	2 h	89
6[b]		**7**	2 h	92
7[c]		**8**	3 h	97
8[d]		**9**	30 min	98[e]

Table 2 Application of Thia-Michael Catalysis Conditions to a Variety of Mercaptans (continued)



Entry	Product		Time	Yield[a] (%)
9		**10**	30 min	98
10		**11**	90 min	>99
11[d]		**12**	90 min	71

[a] Yield of pure product.
[b] Thiol (4 equiv) was used.
[c] Thiol (0.25 equiv) was used.
[d] Thiol (1.5 equiv) was used.
[e] A 92:8 mixture of linkage isomers (*S*/*O*) was obtained in a total of 98% yield.

We were pleased to discover such excellent catalytic activity, and so desired to generalize this protocol by extension to a variety of mercaptan nucleophiles. To this end, we studied the reaction of **1** with a variety of structurally and electronically tuned thiols (Table 2). For this study, we opted to employ the use of 1 mol% tetrabutylammonium hydroxide, as we felt it offered an excellent compromise between catalytic loading, physical measurability, and reaction time. We were gratified to see that a wide variety of thiol-containing compounds were well tolerated in this reaction. Whereas the highly electron-deficient (more acidic; pK_a ≈ 4.6) 2,4,5-trichlorobenzenethiol functioned only moderately well in this reaction (entry 3), the much more electron-rich 4-methoxybenzenethiol (less acidic; pK_a ≈ 6.8) was complete almost instantaneously and in quantitative yield (entry 2). This comes in stark contrast to literature reports which indicate that more electron-poor (more acidic) thiols are better substrates for such reactions.[22] With this data in hand, we suspected that less acidic aliphatic thiols (typical pK_a ≈ 10) would be excellent substrates for this reaction. Indeed, the use of benzylic (entry 4; pK_a ≈ 9.9) and other aliphatic thiols (entries 5–10; pK_a values ≈ 10.5, 9.4, 9.4, 9.6, 8.2, 9.1) gave excellent yields and rapid completion times. Gratifyingly, stoichiometric alterations allowed for the controlled formation of either the monomeric (entry 6) or dimeric (entry 7) compounds when ethane-1,2-dithiol was used, furnishing excellent yields. The reaction of 2-mercaptoethanol (entry 8), while rapid and high-yielding, unex-

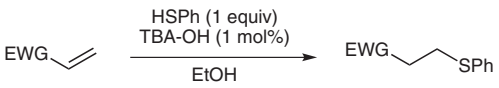
pectedly furnished a 92:8 mixture favoring the *S*-linkage isomer. The use of ethyl 2-mercaptoethanoate provided a nearly quantitative yield of the expected product (entry 9). *N*-Acetyl-protected cysteine also functioned well in this reaction, furnishing an unresolved mixture of diastereomers in essentially perfect yield (entry 10). In agreement with our observations that more acidic thiols gave the opposite of the expected reactivity, using thioacetic acid (entry 11; $pK_a \approx 3.3$) diminished conversion was also observed. In almost all of the above cases, no purification beyond a simple water–diethyl ether partition was required.

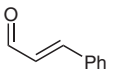
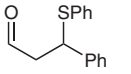
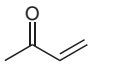
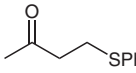
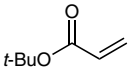
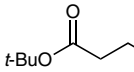
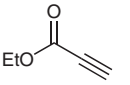
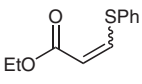
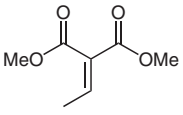
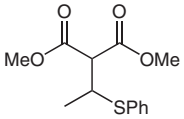
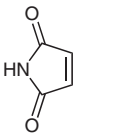
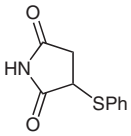
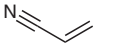
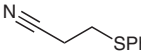
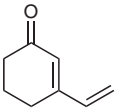
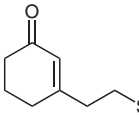
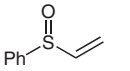
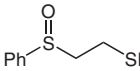
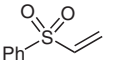
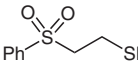
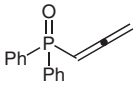
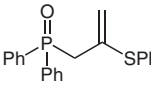
Excited by this initial success, we became interested in extending this methodology to include several additional Michael reaction acceptors. To this end, we considered the reaction of benzenethiol with a variety of Michael acceptor groups-both classical and non-classical (Table 3).

As can be seen from Table 3, a wide variety of both classical (entries 1–7) and non-classical (entries 8–11) Michael systems were readily reactive under the reaction conditions. For example, simple α,β-unsaturated carbonyls (entries 1–3) underwent smooth Michael addition, even with a high degree of steric hindrance at the β-position (entry 1). In the case of methyl vinyl ketone (MVK), a significant degree of polymerization occurred (entry 2). Excellent chemoselectivity was obtained in the reaction with ethyl propiolate (entry 4), as monoaddition occurred exclusively. In accord with literature reports,[23] the *Z*-isomer was the major product. The addition onto other acceptors such as dimethyl ethylidenemalonate (entry 5), succinimide (entry 6), and acrylonitrile (entry 7) were very facile, providing essentially quantitative yields in each case. As expected, the addition onto 3-vinylcyclohex-2-en-1-one provided the 1,6-addition product exclusively (entry 8). While the addition onto phenyl vinyl sulfoxide partially functioned (entry 9), it did not complete, even under extended reaction times.[24] Conversely, the reaction with phenyl vinyl sulfone was nearly flawless, providing quantitative yield of the expected product within two hours. Likewise, the reaction of benzenethiol with allenyldiphenylphosphine oxide (entry 11) also proceeded in excellent yield. While the Michael reactions of this particular compound with the four principle chalogenides have been previously described,[25] only moderate yields were obtained in each case, and the use of preformed anions was a requisite. As such, this current procedure offers significant improvements in accessing these types of compounds. Just as with the previous group of compounds, the majority of these products required no additional purification beyond a simple water–diethyl ether partition to provide analytically pure compound.

In conclusion, we have demonstrated that the use of tetrabutylammonium hydroxide in extremely low catalytic loadings can catalyze the thia-Michael reactions of a wide variety of mercaptans with both classical and non-classical Michael acceptors. This remarkably simple methodology, which usually required no tedious workup or chromatographic purification procedures, provides access to a wide range of molecular scaffoldings rapidly in very high yields and in an environmentally friendly manner. We feel as though this novel methodology is an excellent expansion upon existing catalytic options and will provide chemists with an additional synthetic tool.

Table 3 Extension of Thia-Michael Reaction of Benzenethiol to Additional Michael Acceptors



Entry	Michael acceptor	Product		Time (h)	Yield[a] (%)
1			**13**	7 h	>99
2			**14**	3 h	72[d]
3			**15**	4 h	59[e]
4			**16**	10 min	>99[f]
5			**17**	4 h	99
6			**18**	1 min	>99
7			**19**	1 h	>99
8			**20**	2 h	>99
9			**21**	35 h	69[e]
10			**22**	2 h	99
11			**23**	2 h	99

[a] Yield of pure compound.
[b] 5 mol% catalyst was used.
[c] MVK (1.5 equiv) was used.
[d] A significant amount of polymerization occurred.
[e] The reaction did not complete under the chosen conditions.
[f] The product was obtained as an intractable (*Z*/*E*, 85:15) mixture of geometrical isomers.

All reagents were purchased from Sigma-Aldrich, Fisher-Acros, Strem Chemical, or Alfa-Aesar, and were used without further purification unless otherwise noted. All reactions were performed at r.t. All TLC analysis was performed using 60Å, Glass-backed TLC plates (250 μm thickness, F-254 indicator); PMA = phosphomolybdic acid. ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded at r.t., on either Varian Inova 300 MHz, Bruker ARX400, or Bruker DRX500 spectrometers referenced to either the deuterated residual solvent peak, or to TMS.

TBA-OH-Catalyzed Thia-Michael Addition 2–23; General Procedure

Into a round-bottom flask charged with a magnetic stirbar was added an appropriate Michael acceptor (1.0 equiv). This material was dissolved in enough EtOH to produce a 0.1 M solution. After stirring to ensure dissolution, mercaptan (1.0 equiv) was added, and the mixture was stirred until homogenous. After this time, TBA-OH (40 wt% in H_2O, 1 mol%) was added in one portion, and the mixture was stirred until deemed complete by TLC analysis. The mixture was then partitioned between deionized H_2O (50 mL) and Et_2O (50 mL). After removing the organic layer, the residual product was extracted from the aqueous layer using an additional portion of Et_2O (50 mL). The combined organic layers were then washed with deionized H_2O (50 mL) then brine (50 mL). After drying ($MgSO_4$), the crude product was concentrated under reduced pressure, then, if necessary, purified via column chromatography.

3-(Phenylthio)cyclopentan-1-one (2)[4a]

Yield: 58 mg (>99%); R_f = 0.46 (hexane–EtOAc, 85:15, stain = PMA, *p*-anisaldehyde, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.24 (m, 5 H), 3.89 (p, *J* = 6.0 Hz, 1 H), 2.60 (dd, *J* = 18.7, 7.7 Hz, 1 H), 2.48 (dt, *J* = 18.2, 7.6 Hz, 1 H), 2.38–2.17 (m, 3 H), 2.02 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 216.3, 134.2, 131.9, 129.1, 127.4, 45.2, 43.3, 36.7, 29.3.

LRMS (ESI+): *m*/*z* $[M + Na]^+$ calcd: 215.0; found: 215.0.

3-[(4-Methoxyphenyl)thio]cyclopentan-1-one (3)[15]

Yield: 271 mg (>99%); R_f = 0.53 (hexane–EtOAc, 70:30, stain = *p*-anisaldehyde, vanillin, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39 (d, *J* = 8.7 Hz, 2 H), 6.86 (d, *J* = 8.7 Hz, 2 H), 3.80 (s, 3 H), 3.72 (p, *J* = 6.1 Hz, 1 H), 2.55–2.41 (m, 2 H), 2.31–2.15 (m, 3 H), 1.97 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 216.8, 159.9, 135.8, 124.1, 114.8, 55.4, 45.2, 44.8, 36.9, 29.3.

LRMS (ESI+): *m*/*z* $[M + Na]^+$ calcd: 245.1; found: 245.1.

3-[(2,4,5-Trichlorophenyl)thio]cyclopentan-1-one (4)

Yield: 263 mg (73%); R_f = 0.46 (hexane–EtOAc, 80:20, stain = PMA, *p*-anisaldehyde, $KMnO_4$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.58 (s, 1 H), 7.50 (s, 1 H), 4.06 (m, 1 H), 2.76 (dd, *J* = 18.6, 7.3 Hz, 1 H), 2.65–2.30 (m, 4 H), 2.13 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 214.9, 134.4, 134.0, 131.9, 131.6, 131.1, 44.9, 42.4, 36.8, 29.3.

LRMS (ESI+): *m*/*z* $[M + Na]^+$ calcd: 316.9; found: 317.0; $[M + Na + 2]^+$ calcd: 318.9; found: 319.0; $[M + Na + 4]^+$ calcd: 320.9; found: 321.0.

3-{[(4-Methoxyphenyl)methyl]thio}cyclopentan-1-one (5)

Yield: 260 mg (90%); R_f = 0.50 (hexane–EtOAc, 70:30, stain = PMA, *p*-anisaldehyde, $KMnO_4$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.18 (d, *J* = 8.6 Hz, 2 H), 6.79 (d, *J* = 8.6 Hz, 2 H), 3.72 (s, 3 H), 3.67 (d, *J* = 3.9 Hz, 2 H), 3.21 (p, *J* = 6.9 Hz, 1 H), 2.48–2.03 (m, 5 H), 1.85 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 216.1, 158.4, 129.6, 129.5, 113.7, 55.1, 45.4, 39.5, 37.0, 35.1, 29.5.

LRMS (ESI+): *m*/*z* $[M + Na]^+$ calcd: 259.1; found: 259.1.

3-(Hexylthio)cyclopentan-1-one (6)

Yield: 216 mg (89%); R_f = 0.73 (hexane–EtOAc, 70:30, stain = PMA, *p*-anisaldehyde, $KMnO_4$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.46 (p, *J* = 6.9 Hz, 1 H), 2.64–2.54 (m, 3 H), 2.49–2.31 (m, 2 H), 2.20 (m, 2 H), 1.96 (m, 1 H), 1.60 (p, *J* = 7.1 Hz, 2 H), 1.44–1.27 (m, 6 H), 0.89 (t, *J* = 6.8 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 216.2, 45.8, 40.4, 37.1, 31.4, 31.3, 29.9, 29.6, 28.6, 22.5, 14.1.

LRMS (ESI+): *m*/*z* $[M + Na]^+$ calcd: 223.1; found: 223.1.

3-[(2-Mercaptoethyl)thio]cyclopentan-1-one (7)

Yield: 198 mg (92%); R_f = 0.45 (hexane–EtOAc, 70:30, stain = PMA, *p*-anisaldehyde, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.50 (p, *J* = 6.3 Hz, 1 H), 2.91–2.73 (m, 4 H), 2.62 (dd, *J* = 18.4, 7.1 Hz, 1 H), 2.50–2.34 (m, 2 H), 2.26–2.18 (m, 2 H), 1.96 (m, 1 H), 1.74 (t, *J* = 7.7 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 216.2, 45.8, 40.5, 37.1, 35.5, 30.1, 24.9.

LRMS (ESI+): *m*/*z* $[M + Na]^+$ calcd: 199.0; found: 199.0.

1,2-Bis[(3-oxocyclopentyl)thio]ethane (8)[7]

Yield: 76 mg (98%); R_f = 0.13 (hexane–EtOAc, 70:30, stain = PMA, *p*-anisaldehyde, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.52 (p, *J* = 6.2 Hz, 2 H), 2.82 (s, 4 H), 2.63 (dd, *J* = 18.2, 6.8 Hz, 2 H), 2.50–2.37 (m, 4 H), 2.27–2.19 (m, 4 H), 1.98 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 216.1, 45.8, 40.7, 37.1, 31.6, 30.1.

LRMS (ESI+): *m*/*z* $[M + Na]^+$ calcd: 281.1; found: 281.0.

3-[(2-Ethoxy-2-oxoethyl)thio]cyclopentan-1-one (10)

Yield: 242 mg (>99%); R_f = 0.41 (hexane–EtOAc, 70:30, stain = PMA, *p*-anisaldehyde, $KMnO_4$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.20 (q, *J* = 7.1 Hz, 2 H), 3.64 (p, *J* = 7.1 Hz, 1 H), 3.29 (m, 2 H), 2.66 (dd, *J* = 18.5, 7.4 Hz, 1 H), 2.41 (m, 2 H), 2.23 (m, 2 H), 1.98 (m, 1 H), 1.30 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 216.1, 170.3, 61.6, 45.4, 41.0, 37.2, 33.3, 29.6, 14.3.

LRMS (ESI+): *m*/*z* $[M + Na]^+$ calcd: 225.1; found: 225.0.

Methyl *N*-Acetyl-*S*-(3-oxocyclopentyl)cysteine (11)

Yield: 316 mg (>99%); R_f = 0.38, EtOAc, stain = *p*-anisaldehyde, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.32 (m, 1 H), 4.85 (m, 1 H), 3.79 (s, 3 H), 3.49 (m, 1 H), 3.13–2.98 (m, 2 H), 2.61 (m, 1 H), 2.40 (m, 2 H), 2.19 (m, 2 H), 2.06 (s, 3 H), 1.93 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 215.9, 170.8, 170.3, 52.2, 51.7, 45.1, 40.2, 36.5, 29.3, 26.2, 22.4.

LRMS (ESI+): *m*/*z* $[M + Na]^+$ calcd: 282.1; found: 282.1.

3-(Acetylthio)cyclopentan-1-one (12)[26]

Yield: 137 mg (71%); R_f = 0.53 (hexane–EtOAc, 70:30, stain = I_2, *p*-anisaldehyde, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.99 (p, *J* = 7.3 Hz, 1 H), 2.67 (dd, *J* = 18.7, 7.7 Hz, 1 H), 2.46–2.29 (m, 2 H), 2.28 (s, 3 H), 2.26–2.10 (m, 2 H), 1.91 (s, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 215.7, 195.2, 44.6, 39.2, 37.6, 30.6, 29.6.

LRMS (ESI+): *m*/*z* $[M + Na]^+$ calcd: 181.0; found: 181.0.

3-Phenyl-3-(phenylthio)propanal (13)[27]
Yield: 184 mg (>99%); R_f = 0.61 (hexane–EtOAc, 70:30, stain = I_2, *p*-anisaldehyde, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.62 (s, 1 H), 7.31–7.13 (m, 10 H), 4.68 (t, *J* = 7.4 Hz, 1 H), 2.99 (d, *J* = 7.4 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): 199.4, 140.5, 133.4, 133.3, 129.1, 128.9, 128.6, 127.9, 127.7, 49.1, 47.2.

LRMS (ESI+): *m*/*z* $[M + Na]^+$ calcd: 265.1; found: 265.1.

4-(Phenylthio)butan-2-one (14)[28]
Yield: 185 mg (72%); R_f = 0.51 (hexane–EtOAc, 70:30, stain = *p*-anisaldehyde, $KMnO_4$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.35–7.16 (m, 5 H), 3.13 (t, *J* = 7.2 Hz, 2 H), 2.75 (t, *J* = 7.3 Hz, 2 H), 2.14 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.3, 135.5, 129.3, 128.8, 126.1, 43.0, 30.1, 27.4.

LRMS (ESI+): *m*/*z* $[M + Na]^+$ calcd: 203.1; found: 203.0.

***tert*-Butyl 3-(Phenylthio)propanoate (15)[29]**
Yield: 140 mg (59%); R_f = 0.33 (hexane–CH_2Cl_2, 60:40, stain = $KMnO_4$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.37–7.15 (m, 5 H), 3.12 (t, *J* = 7.4 Hz, 2 H), 2.53 (t, *J* = 7.4 Hz, 2 H), 1.44 (s, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.8, 135.5, 129.9, 128.9, 126.3, 80.9, 35.6, 29.3, 28.2.

LRMS (ESI+): *m*/*z* $[M + Na]^+$ calcd: 261.1; found: 261.1; $[M + K]^+$ calcd: 277.1; found: 277.1.

Ethyl (*Z*)-3-(Phenylthio)prop-2-enoate (16)[23]
Yield: 318 mg (>99%); R_f = 0.56 (hexane–EtOAc, 80:20, stain = $KMnO_4$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.44–7.26 (m, 6 H), 7.21 (d, *J* = 10.1 Hz, 1 H), 5.87 (d, *J* = 10.1 Hz, 1 H), 4.20 (q, *J* = 7.1 Hz, 2 H), 1.27 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.2, 149.4, 135.9, 130.8, 129.1, 128.0, 113.2, 60.2, 14.4.

LRMS (ESI+): *m*/*z* $[M + Na]^+$ calcd: 231.0; found: 231.0.

Dimethyl 2-[1-(Phenylthio)ethyl]malonate (17)
Yield: 168 mg (99%); R_f = 0.52 (hexane–$CHCl_3$, 30:70, stain = PMA, *p*-anisaldehyde, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.26 (m, 5 H), 3.79–3.65 (m, s, s, 2 H, 3 H, 3 H), 3.55 (d, *J* = 8.7 Hz, 1 H), 1.36 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 167.9, 167.6, 133.8, 132.7, 128.9, 128.0, 57.3, 52.5, 52.5, 42.9, 19.1.

LRMS (ESI+): *m*/*z* $[M + Na]^+$ calcd: 291.1; found: 291.1.

2-(Phenylthio)succinimide (18)[30]
Yield: 219 mg (>99%); R_f = 0.38 (hexane–EtOAc, 70:30, stain = *p*-anisaldehyde, I_2, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.38 (s, 1 H), 7.49–7.32 (m, 5 H), 4.08 (dd, *J* = 9.1, 4.4 Hz, 1 H), 3.14 (dd, *J* = 18.8, 9.1 Hz, 1 H), 2.66 (dd, *J* = 18.8, 4.4 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 176.8, 175.8, 133.8, 130.6, 129.4, 129.0, 45.2, 37.1.

LRMS (ESI+): *m*/*z* $[M + Na]^+$ calcd: 230.0; found: 230.1.

3-(Phenylthio)propionitrile (19)[31]
Yield: 163 mg (>99%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46 (s, 6 H), 3.05 (t, *J* = 7.0 Hz, 2 H), 2.55 (t, *J* = 7.0 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 133.1, 131.0, 129.2, 127.4, 118.1, 29.9, 18.0.

LRMS (ESI+): *m*/*z* $[M + Na]^+$ calcd: 186.0; found: 186.1.

3-[2-(Phenylthio)ethyl]cyclohex-2-en-1-one (20)[32]
Yield: 201 mg (>99%); R_f = 0.28 (hexane–EtOAc, 80:20, stain = vanillin, $KMnO_4$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25–7.06 (m, 5 H), 5.78 (s, 1 H), 2.96 (t, *J* = 7.5 Hz, 2 H), 2.41 (t, *J* = 7.5 Hz, 2 H), 2.24 (t, *J* = 5.9 Hz, 2 H), 2.16 (t, *J* = 5.8 Hz, 2 H), 1.85 (p, *J* = 5.9 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 199.0, 163.1, 135.3, 129.5, 128.8, 126.4, 126.2, 37.3, 37.2, 31.0, 29.4, 22.5.

LRMS (ESI+): *m*/*z* $[M + Na]^+$ calcd: 255.1; found: 255.1.

Phenyl 2-(Phenylthio)ethyl Sulfone (22)[33]
Yield: 248 mg (>99%); R_f = 0.35 (hexane–EtOAc, 75:25, stain = PMA, *p*-anisaldehyde, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 7.8 Hz, 2 H), 7.62 (m, 1 H), 7.52 (t, *J* = 7.6 Hz, 2 H), 7.23–7.18 (m, 5 H), 3.30 (m, 2 H), 3.14 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 138.3, 133.9, 133.3, 129.8, 129.3, 129.1, 127.9, 126.9, 55.4, 26.1.

LRMS (ESI+): *m*/*z* $[M + Na]^+$ calcd: 301.0; found: 301.0.

Diphenyl[2-(phenylthio)prop-2-en-1-yl]phosphine Oxide (23)[25a]
Yield: 290 mg (>99%); R_f = 0.44 (hexane–EtOAc, 50:50, stain = PMA, *p*-anisaldehyde, $KMnO_4$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.70–7.64 (m, 4 H), 7.41–7.29 (m, 6 H), 7.19–7.10 (m, 5 H), 5.45 (d, *J* = 3.8 Hz, 1 H), 4.98 (d, *J* = 3.9 Hz, 1 H), 3.19 (d, $J_{H\text{-}P}$ = 13.2 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 134.5 (d, $J_{C\text{-}P}$ = 9.0 Hz), 132.6, 132.1, 131.6, 131.3, 130.8, 130.7, 128.9, 128.2, 128.1, 127.8, 118.3, 37.4, 37.2 (d, $J_{C\text{-}P}$ = 65.3 Hz).

^{31}P NMR (121 MHz, $CDCl_3$): δ = 29.2.

LRMS (ESI+): *m*/*z* $[M + Na]^+$ calcd: 373.1; found: 373.1.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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