2-[[(p-Nitrophenyl)sulfonyl]oxy] 3-Keto Esters as Intermediates for the Regiospecific Preparation of 2-[[(p-Nitrophenyl)sulfonyl]oxy] Ketones

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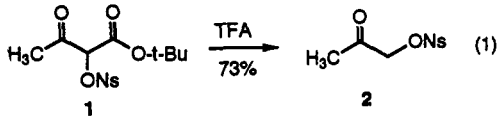
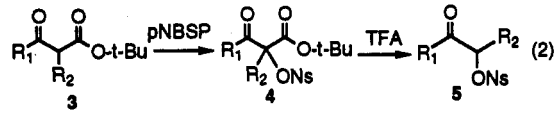
It has been previously shown that 2-[(p-nitrophenyl)-sulfonyl]oxy] 3-keto esters[1] are very useful synthetic intermediates for the synthesis of a variety of densely functionalized compounds including tricarbonyl esters,[2] tricarbonyl amides,[3] 3-hydroxy-2-(nosyloxy) esters,[4] and 3-hydroxy-2-azido esters.[4] An additional application briefly described in the initial report was the use of 2-(nosyloxy)-β-keto ester 1 for the synthesis of α-nosyloxy ketone 2 (eq 1).[1]



1 2 (1)

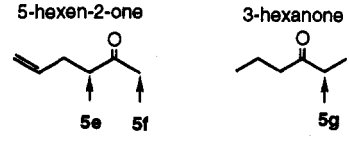
This reaction provides the basis for a new strategy for the preparation of α-(nosyloxy) ketones.[5] Interest in this strategy was fueled by observations that α-(nosyloxy) ketones have quite interesting properties as compared to the analogous α-bromo ketones. The electron-withdrawing ability of the nosyloxy group simplifies the chemistry significantly by activating the carbonyl group toward addition by nucleophiles. In the presence of potassium carbonate in methanol or amines, α-(nosyloxy)ketones undergo smooth conversion to α-hydroxy ketals and α-hydroxy ketones or α-amino ketones, respectively.[6] The regiochemistry of these products is the same as that of the starting α-(nosyloxy) ketone; hence, regiochemical control in the preparation of α-(nosyloxy) ketones guarantees regiospecificity in the derived products. The conversion of *tert*-butyl β-keto esters 3 to their 2-(nosyloxy) derivatives 4 followed by decarboxylation could give α-(noxyloxy) ketones 5 whose regiochemistry is dictated by the substituents present in the starting β-ketoester (eq 2).



3 4 5 (2)

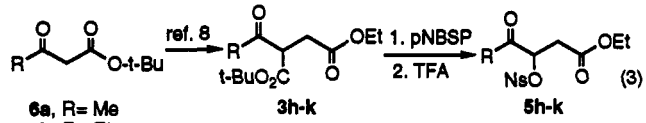
Previous regiospecific preparations of α-(nosyloxy) ketones were based on enol or enamine derivatives of ketones reacting with (p-nitrophenyl)sulfonyl peroxide (pNBSP).[6] Such preparations are not without their difficulties, however, and many enol derivatives could not be produced in regiochemically pure form.[7] The chemistry shown in eq 2 could circumvent many of these difficulties since the *tert*-butoxycarbonyl group effectively directs installation of the nosylate group by pNBSP and is then removed.

To demonstrate this approach, a series of *tert*-butyl β-keto esters 3 was treated with pNBSP and zinc(II) chloride[8] in ethyl acetate to furnish α-(nosyloxy) β-keto esters 4. Decarboxylation with TFA gave nosyloxy ketones 5 regiospecifically. The results are shown in Table 1. Fair to good overall yields were obtained for all substrates examined. The intermediate α-(nosyloxy) β-keto ester can be isolated and then decarboxylated in a subsequent step (Table 1, compounds **4a–d**); however, a more convenient procedure is to decarboxylate this intermediate without isolation (Table 1, compounds **4e,f,g**). The regiochemical control that can be achieved by this approach is illustrated by the data as well. For example, regioisomers **5e** and **5f** are synthetically equivalent to the



delivery of the nosyloxy group to C-1 or C-3 of 5-hexen-2-one, respectively. They are prepared regiochemically pure by the present procedure from **3e** and **3f**, respectively. Likewise, the preparation of **5g** is the synthetic equivalent of distinguishing the ethyl and *n*-propyl groups of 3-hexanone for attaching the nosyloxy group. Such regiochemical control would be virtually impossible using methodology tied to enol or enolate formation.

The same strategy can be used for the regiospecific preparation of 3-(nosyloxy)-4-keto esters **5h–k**. Alkylation of keto esters **6a–d** with ethyl bromoacetate gave the known ketodiesters **3h–k**.[8] Reaction of **3h–k** with pNBSP followed by decarboxylation with TFA gave 3-(nosyloxy)-4-keto esters **5h–k** in good yields (eq 3).



6a, R= Me
6b, R= Et
6c, R= n-Pr
6d, R= i-Pr

3h-k **5h-k** (3)

While substitution reactions of **5h–k** could potentially lead to 3-substituted 4-keto esters, keto esters **5h–k** could also undergo elimination to α,β-unsaturated γ-keto esters. For example, alkylation of *tert*-butyl acetoacetate with optically active bromoacetates **7a** and **7b** followed by attachment of the nosyloxy group with pNBSP and decarboxylation with TFA gave 3-(nosyloxy)-4-keto esters **8a,b** which appeared to be somewhat unstable to chromatography and were carried on immediately. Diastereomers of both **8a** and **8b** were evident in the ^{1}H NMR from the two singlets found for the methoxy groups, but in neither **8a** nor **8b** was significant diastereoselectivity observed. Treatment of **8a,b** with triethylamine provided unsaturated keto esters **9a,b** (eq 4).

The 4-keto-2-alkenoate subunit highlighted in **9** (eq 4) is found in a variety of natural products having interesting

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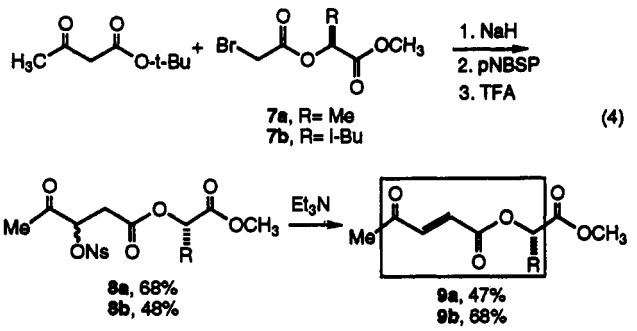
Table 1. Yields for the Conversion of *tert*-Butyl β-Keto Esters 3 to Their 2-(Nosyloxy) Derivatives 4 and Then α-(Nosyloxy) Ketones 5

	3			
	R_1	R_2	4 (%)	5 (%)
a	Ph	H	55	92 (51)[c]
b	$PhCH_2CH_2$	H	71	93 (66)[c]
c	C_6H_{11}	H	67	90 (60)[c]
d	C_6H_{11}	CH_3	82	98 (80)[c]
e	CH_2=$CHCH_2CH_2$	H	*b*	68[d]
f	CH_3	CH_2CH=CH_2	*b*	41[d]
g	n-Pr	CH_3	*b*	47[d]
h	CH_3	CH_2CO_2Et	*b*	59[d]
i	Et	CH_2CO_2Et	*b*	61[d]
j	n-Pr	CH_2CO_2Et	*b*	69[d]
k	i-Bu	CH_2CO_2Et	*b*	76[d]

[a] Yields are for isolated yields of analytically pure products. [b] Intermediate 2-(nosyloxy) β-keto ester not isolated. [c] Yield in parentheses is the overall yield for the two-step sequence of 3 → 4 → 5. [d] Yield is for the conversion of 3 → 5 without isolation of 4.



(4)

biological properties.[9] The antifungal agents (*R,R*)-pyrenophorin[10] and (*R*)-patulolide[11] are both macrocyclic lactones which contain the chiral ester of a 4-keto-2-alkenoate in their structure. Their biological activity has engendered a good deal of interest in the preparation of these compounds and analogs containing this functional grouping.[9b,12] The 4-keto-2-alkenoate subunit can also be elaborated into ketoethylene peptide isosteres which are also of interest as peptidase inhibitors.[13]

The installation of the 4-keto-2-alkenoate subunit is usually achieved by protecting the ketone and then generating the double bond by either by selenation–elimination[12b-d] or by a Wittig reaction[12a] using carbanion methodology. The present approach provides a simple and effective entry into this class of molecules and provides a very useful alternative to current methods since the ketone need not be protected and the double bond is installed under very mild conditions.

Experimental Section

Melting points were obtained on a Mel Temp apparatus and are uncorrected. Infrared spectral data (Perkin-Elmer 283) are reported in cm^{-1}. Chemical shifts for both proton NMR spectra (200 or 400 MHz) and ^{13}C NMR spectra (100 MHz) are reported for chloroform-*d* solutions in ppm relative to Me_4Si. Elemental analyses were performed by M-H-W Laboratories, Phoenix, AZ. Thin-layer chromatography was performed on silica gel 60 F254 plates from EM reagents and visualized by UV irradiation/or iodine vapor. Flash column chromatography was performed using silica gel 60 (230–400 mesh). Reaction mixtures were often vacuum filtered through a shoft (2.5 cm) pad of silica gel which was covered with a layer of magnesium sulfate (0.5 cm). This served to both dry the reaction mixture and remove polar impurities. Starting β-keto esters **3** were either purchased from Aldrich or prepared by literature procedures.[14] Starting materials **3h–k** were prepared by literature methods.[8] pNBSP was prepared by the standard method.[15]

General Procedure for the Preparation of 2-[((*p*-Nitrophenyl)sulfonyl]oxy] β-Keto Esters. To a room-temperature solution of pNBSP (3.0 mmol) in ethyl acetate (80 mL) was added $ZnCl_2$ (3.0 mmol). The mixture was stirred for about 20 min until it became homogeneous. The β-keto ester **3** (3.0 mmol) in ethyl acetate (10 mL) was added to the clear solution. After 1 h the mixture was washed with water (50 mL) and brine (50 mL), and the organic layer was separated and dried over $MgSO_4$. The solvent was evaporated *in vacuo*, and the crude product was purified by recrystallization from MeOH or ethyl ether.

***tert*-Butyl 2-[((*p*-Nitrophenyl)sulfonyl)oxy]-3-oxo-3-phenylpropanoate, 4a,** was prepared from *tert*-butyl-3-oxobenzoate (3.0 mmol) as a white solid in 55% yield after recrystallization from MeOH: mp 139–140 °C; ^1H NMR ($CDCl_3$) δ 1.35 (s, 9H, $(CH_3)_3C$), 6.04 (s, 1H, CH), 7.46–8.36 (m, 9H, aromatic H); IR (KBr) 3096, 2997, 1756, 1689, 1383, 1352, 1060 cm^{-1}. Anal. Calcd for $C_{19}H_{19}NO_8S$: C, 54.15; H, 4.54; N, 3.32. Found: C, 54.37; H, 4.77; N, 3.57.

***tert*-Butyl 2-[((*p*-Nitrophenyl)sulfonyl)oxy]-3-oxo-5-phenylpentanoate, 4b,** was prepared from *tert*-butyl-3-oxophenylpentanoate (3.0 mmol) as a white solid in 71% yield after recrystallization from ethyl ether: mp 97–98 °C; ^1H NMR ($CDCl_3$) δ 1.38 (s, 9H, $(CH_3)C$), 2.88–2.97 (m, 4H, $-CH_2CH_2-$), 5.27 (s, 0.5H, CH keto tautomer), 7.14–7.32 (m, 5H, aromatic H), 8.27 (AB q, 4H, J = 9.02 Hz, aromatic H); IR (KBr) 3107, 2977, 1762, 1737, 1604, 1533, 1381, 1352, 1193 cm^{-1}. Anal. Calcd for $C_{21}H_{23}NO_8S$: C, 56.11; H, 5.16; N, 3.12. Found: C, 56.21; H, 5.11; N, 3.28.

***tert*-Butyl 2-[((*p*-Nitrophenyl)sulfonyl)oxy]-3-oxo-3-cyclohexylpropanoate, 4c,** was prepared from *tert*-butyl-3-oxo-3-cyclohexylpropanoate (3.0 mmol) as a white solid in 67% yield after recrystallization from MeOH: mp 119–120 °C; ^1H NMR ($CDCl_3$) δ 1.21–1.81 (m, 10H, cyclohexyl H's), 1.43 (s, 9H, $(CH_3)_3C$), 2.70–2.86 (m, 1H, CH), 5.44 (s, 0.6H, keto tautomer), 8.30 (AB q, 4H, J = 8.99 Hz, aromatic H); IR (KBr) 3116, 2947, 1771, 1740, 1357, 1317, 1202 cm^{-1}. Anal. Calcd for $C_{19}H_{25}NO_8S$: C, 53.38; H, 5.90; N, 3.28. Found: C, 53.27; H, 5.98; N, 3.26.

***tert*-Butyl 2-Methyl-2-[((*p*-nitrophenyl)sulfonyl)oxy]-3-oxo-3-cyclohexylpropanoate, 4d,** was prepared from *tert*-butyl 2-methyl-3-oxocyclohexanoate (3.0 mmol) as a white solid in 82% yield after recrystallization from MeOH: mp 94–96 °C; ^1H NMR ($CDCl_3$) δ 1.25–1.82 (m, 10H, cyclohexyl H's), 1.51 (s, 9H, $(CH_3)_3C$), 1.88 (s, 3H, CH_3), 5.31 (s, 0.5H, CH (keto tautomer)), 8.31 (AB q, 4H, J = 8.88 Hz, aromatic H); IR (KBr) 3109, 2935, 1756, 1736, 1370, 1355, 1193 cm^{-1}. Anal. Calcd for $C_{20}H_{27}NO_8S$: C, 54.41; H, 6.17; N, 3.17. Found: C, 54.41; H, 6.24; N, 3.21.

General Procedure for the Decarboxylation of 2-[((*p*-Nitrophenyl)sulfonyl)oxy] β-Keto Esters. The 2-nosyl-3-keto ester **4** (0.4–0.7 mmol) was dissolved in 15 mL of CH_2Cl_2, 2 mL of trifluoroacetic acid was added, and the mixture was stirred for 3 h. The solvent was evaporated in vacuo, and the residue was taken up in dichloromethane (20 mL), washed with water (20 mL), and passed through a short pad of magnesium sulfate and silica gel. Evaporation of solvent provided the α-(nosyloxy) ketone product.

[((*p*-Nitrophenyl)sulfonyl)oxy]acetophenone, 5a, was obtained as a white solid in 92% yield: mp 128–130 °C; ^1H NMR ($CDCl_3$) δ 5.49 (s, 2H, CH_2), 7.47–8.41 (m, 9H, aromatic H); IR

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(KBr) 3112, 2931, 1740, 1604, 1592, 1378, 1354, 1191 cm^{-1}. Anal. Calcd for $C_{14}H_{11}NO_6S$: C, 52.33; H, 3.45; N, 4.36. Found: C, 52.33; H, 3.66; N, 4.34.

[((*p*-Nitrophenyl)sulfonyl)oxy]-4-phenyl-2-butanone, 5b, was obtained as a white solid in 93% yield: mp 53–55 °C; ^{1}H NMR ($CDCl_3$) δ 2.77–2.92 (m, 4H, CH_2CH_2), 4.65 (s, 2H, CH_2), 7.13–8.40 (m, 9H, aromatic H); IR (KBr) 3116, 2957, 1710, 1526, 1374, 1349, 1186 cm^{-1}. Anal. Calcd for $C_{16}H_{15}NO_6S$: C, 55.00; H, 4.33; N, 4.01. Found: C, 54.83; H, 4.37; N, 4.03.

2-[((*p*-Nitrophenyl)sulfonyl)oxy]-1-cyclohexylethanone, 5c, was obtained as a white solid in 90% yield: mp 110–111 °C; ^{1}H NMR ($CDCl_3$) δ 1.26–1.85 (m, 10H, Cy H), 2.42–2.46 (m, 1H, Cy H), 4.84 (s, 2H, CH_2), 8.30 (AB q, 4H, J = 2.09 Hz, aromatic H); IR (KBr) 3107, 2930, 1720, 1531, 1377, 1352, 1191 cm^{-1}. Anal. Calcd for $C_{14}H_{17}NO_6S$: C, 51.36; H, 5.24; N, 4.28. Found: C, 51.54; H, 5.38; N, 4.16.

2-[((*p*-Nitrophenyl)sulfonyl)oxy]-1-cyclohexyl-1-propanone, 5d, was obtained as a white solid in 98% yield: mp 123–124 °C; ^{1}H NMR ($CDCl_3$) δ 1.21–1.85 (m, 10H, Cy H), 1.45 (d, 3H, J = 6.98 Hz), 2.05–2.63 (m, 1H, Cy CH), 5.20 (q, 1H, J = 7.06 Hz, CH), 8.29 (AB q, 4H, J = 2.09 Hz, aromatic H); IR (KBr) 2930, 1729, 1544, 1371, 1353, 1188 cm^{-1}. Anal. Calcd for $C_{15}H_{19}NO_6S$: C, 52.77; H, 5.61; N, 4.10. Found: C, 52.34; H, 5.58; N, 4.10.

General Procedure for the Two-Step Conversion of β-Keto Esters 3 to α-(Nosyloxy) Ketones 5. pNBSP (1.21 g, 3 mmol) and zinc chloride (870 mg, 3 mmol) were added to a cooled (0 °C) solution of the keto ester (3 mmol) in ethyl acetate (80 mL). The resulting mixture was stirred at 0 °C for 3 h and at room temperature overnight. The resulting solution was washed with 1 N HCl (100 mL) and brine (100 mL) and passed through a short pad of $MgSO_4$ and silica gel 60 to provide an oil. This oil was treated with TFA (3 mL) at room temperature for 3 h. After dilution with ethyl acetate (50 mL), the solution was washed with H_2O (50 mL) and 1 N HCl (50 mL) and passed through a short pad of $MgSO_4$ and silica 60 to provide the crude α-(nosyloxy) ketone which was purified by chromatography on silica gel.

1-[((*p*-Nitrophenyl)sulfonyl)oxy]-5-hexen-2-one, 5e, was prepared from **3e** in 68% yield after purification by radial chromatography (hexane/ethyl acetate (95:5 to 90:10 to 80:20)) as a white solid: mp 58–59 °C; NMR (200 MHz, $CDCl_3$) δ 2.34 (q, 2H, J = 7.0 Hz, CH_2=CHCH_2CH_2–), 2.56 (t, 2H, J = 7.0 Hz, CH_2=CHCH_2CH_2–), 4.73 (s, 2H, –CHONs), 4.99 (set of m, 2H, CH_2=CH–), 5.75 9m, 1H, CH_2=CH–), 8.16 and 8.43 (ABq, 4H, aromatic H); IR (neat) 3080, 2950, 2905, 1725, 1520, 1340, 1180 cm^{-1}. Anal. Calcd for $C_{12}H_{13}NO_6S$: C, 48.15; H, 4.38; N, 4.68. Found: C, 47.95; H, 4.41; N, 4.68.

3-[((*p*-Nitrophenyl)sulfonyl)oxy]-5-hexen-2-one, 5f, was prepared from **3f** in 41% yield after purification by radial chromatography (hexane/ethyl acetate (95:5 to 80:20)) as a white solid: mp 46–47 °C; NMR ($CDCl_3$, 400 MHz) δ 2.25 (s, 3H, O=CCH_3), 2.55 (m, 2H, CH_2CH=CH_2), 4.91 (dt, 1H, J = 5.6, 5.2 Hz, CHONs), 5.06 (d, 1H, J = 9.2 Hz, CH=CH_2), 5.09 (d, 1H, J = 15.6 Hz, CH=CH_2), 5.54 (m, 1H, CH=CH_2), 8.15 and 8.43 (ABq, 4H, aromatic H); ^{13}C NMR ($CDCl_3$), 100 MHz) 29.05, 38.30, 87.12, 122.85, 127.11, 132.01, 132.80, 144.45, 152.55, 205.58; IR (neat) 3127, 2947, 1740, 1611, 1540, 1372, 1197 cm^{-1}. Anal. Calcd for $C_{12}H_{13}NO_6S \cdot {}^1/_2H_2O$: C, 46.60; H, 4.56; N, 4.52. Found: C, 47.00; H, 4.67; N, 4.55.

2-[((*p*-Nitrophenyl)sulfonyl)oxy]-3-hexanone, 5g, was prepared from **3g** in 47% yield after purification by radial chromatography (hexane/ethyl acetate (95:5 to 90:10 to 80:20)) as a white solid: mp 62–63 °C (ethyl acetate/hexane); NMR ($CDCl_3$, 200 MHz) δ 0.91 (t, 3H, J = 7.4 Hz, CH_2CH_3), 1.45 (d, 3H, J = 6.8 Hz, CH(ONs)CH_3), 1.60 (m, 2H, J = 7.4 Hz, $CH_2CH_2CH_3$), 2.53 (t, 2H, J = 7.4 Hz, CH_2CH_2CH$_3$), 5.00 (q, 1H, J = 7.0 Hz, CH(ONs)CH$_3$), 8.15 and 8.43 (AB q, 4H, aromatic H); IR (CH_2Cl_2) 3090, 3040, 2950, 1710, 1525, 1345, 1260, 1180 cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO_6S$: C, 47.83; H, 5.02; N, 4.65. Found: C, 47.81; H, 5.06; N, 4.62.

Ethyl 3-[((*p*-Nitrophenyl)sulfonyl)oxy]-4-oxopentanoate, 5h, was prepared from **3h** as a colorless oil in 59% yield after purification by radial chromatography (hexane/ethyl acetate (80:20)): ^{1}H NMR ($CDCl_3$) δ 1.220 (t, 3H, J = 6.8 Hz, OCH_2CH_3), 2.35 (s, 3H, CH_3C=O), 2.86 (ABq, 2H, J = 6.0 Hz, CH_2COOEt), 4.05 (q, 2H, J = 6.8 Hz, OCH_2CH$_3$), 5.19 (dd, 1H, J = 6.0 Hz, CHONs), 8.16 and 8.44 (AB q, 4H, aromatic H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.01, 26.63, 36.51, 61.57, 80.81, 124.50, 129.45, 141.67, 151.01, 168.34, 202.87. Anal. Calcd for $C_{13}H_{15}NO_8S$: C, 45.22; H, 4.38; N, 4.06. Found: C, 45.37; H, 4.47; N, 3.95.

Ethyl 3-[[(*p*-Nitrophenyl)sulfonyl)oxy]-4-oxohexanoate, 5i, was prepared from **3i** as a colorless oil in 61% yield after purification by radical chromatography (hexane/ethyl acetate (95:5)): ^{1}H NMR ($CDCl_3$) δ 1.09 (t, 3H, J = 7.0 Hz, CH_2CH_3), 1.19 (t, 3H, J = 6.4 Hz, OCH_2CH_3), 2.72 (m, 2H, J = 6.8 Hz, CH_2CH$_3$), 2.87 (dd, 2H, J = 2.2, 5.8 Hz, CH_2COOEt), 4.04 (q, 2H, J = 6.6 Hz, OCH_2CH$_3$), 5.22 (dd, 1H, J = 6.0 Hz, CHONs), 8.15 and 8.43 (AB q, 4H, aromatic CH); IR (neat) 3108, 2984, 1735, 1535, 1377, 1352, 1188 cm^{-1}; ^{13}C NMR (100 MHz, $CDCl_3$) 7.00, 14.01, 32.31, 36.69, 61.52, 80.69, 124.50, 129.42, 141.75, 151.00, 168.44, 205.46. Anal. Calcd for $C_{14}H_{17}NO_8S$: C, 46.79; H, 4.77; N, 3.90. Found: C, 46.80; H, 4.59; N, 3.91.

Ethyl 3-[(*p*-Nitrophenyl)sulfonyl)oxy]-4-oxoheptanoate, 5j, was prepared from **3j** as a colorless oil in 69% yield after purification by flash chromatography (hexane/ethyl acetate (95:5 to 90:10)): ^{1}H NMR ($CDCl_3$) δ 0.92 (t, 3H, J = 7.2 Hz, $CH_2CH_2CH_3$), 1.19 (t, 3H, J = 7.2 Hz, OCH_2CH_3), 1.62 (sextet, 2H, J = 7.2 Hz, $CH_2CH_2CH_3$), 2.64 (d of t, 2H, J = 3.6, 7.2 Hz, CH_2CH$_2$CH$_3$), 2.85 (two d, 2H, J = 6.2 Hz, CH_2COOEt), 4.05 (q, 2H, J = 7.0 Hz, OCH_2CH$_3$), 5.22 (dd, 1H, J = 3.6, 6.2 Hz, CHONs), 8.16 and 8.44 (AB q, 4H, aromatic H); IR (neat) 3108, 2966, 1736, 1536, 1376, 1351, 1189 cm^{-1}; ^{13}C NMR (100 MHz, $CDCl_3$) 13.52, 14.03, 16.38, 36.51, 40.64, 61.53, 80.77, 124.50, 129.46, 141.80, 151.01, 168.43, 204.69. Anal. Calcd for $C_{15}H_{19}NO_8S$: C, 48.25; H, 5.13; N, 3.75. Found: C, 48.20; H, 5.24; N, 3.62.

Ethyl 3-[((*p*-Nitrophenyl)sulfonyl)oxy]-5-methyl-4-oxohexanoate, 5k, was prepared from **3k** as a colorless oil in 76% yield after purification by radial chromatography (hexane/ethyl acetate (95:5 to 90:10)): ^{1}H NMR ($CDCl_3$) δ 1.14 (t and d, 9H, J = 7.2, 7.2 Hz, OCH_2CH_3, CH(CH_3)$_2$), 2.86 (d, 2H, J = 5.8 Hz, CH_2COOEt), 3.06 (m, 1H, J = 6.8 Hz, CH(CH$_3$)$_2$), 4.06 (q, 2H, J = 7.0 Hz, OCH_2CH$_3$), 5.45 (t, 1H, J = 5.6 Hz, CHONs), 8.16 and 8.43 (AB q, 4H, aromatic H); IR ($CDCl_3$) 3107, 2980, 1735, 1534, 1378, 1351, 1266, 1187 cm^{-1}; ^{13}C NMR (100 MHz, $CDCl_3$) 14.03, 17.92, 18.27, 36.46, 36.59, 61.53, 79.50, 124.45, 129.39, 141.96, 150.96, 168.44, 207.85. Anal. Calcd for $C_{15}H_{19}NO_8S$: C, 48.25; H, 5.13; N, 3.75. Found: C, 48.48; H, 5.27; N, 3.78.

Preparation of 3-(Nosyloxy) 4-Keto Ester 8a. *tert*-Butyl acetoacetate (790 mg, 5 mmol) was added to a 0 °C suspension of sodium hydride (270 mg, 50% in mineral oil, 5.5 mmol) in THF (30 mL). After the mixture was stirred for 10 min, bromoacetyl ester **7a**[16] (1.12 g, 5 mmol) was added, and the mixture was stirred at 0 °C for 3 h and at room temperature overnight. Addition of 1 N HCl (50 mL) was followed by extraction with ether (3 × 60 mL). The ether extracts were passed through a short pad of $MgSO_4$ and silica gel 60 and evaporated. The residue was distilled by bulb-to-bulb distillation (bath temperature 140–160 °C, 0.5 mmHg) to give a colorless oil (1.42 g, 94%) which was carried on immediately in the next step.

The above oil (910 mg, 3 mmol) was dissolved in ethyl acetate (80 mL) and carried through the two-step procedure of nosylation–decarboxylation described above to give **8a** as a sticky oil (830 mg, 68%) after purification by flash chromatography (hexane/ethyl acetate (95:5 to 80:20)): ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.45 (two d, J = 7.2 Hz, 3H, CHCH_3), 2.36 (s, 3H, CH_3C=O), 2.95 (m, 2H, CH_2CO$_2$), 3.73 (two s, 3H, OCH_3), 4.97 (m, 1H, CHCH$_3$), 5.20 (m, 1H, CHONs), 8.19 and 8.43 (AB q, 4H, aromatic H). Since **8a** appeared to be somewhat unstable to chromatography, it was carried on without further characterization.

4-Oxoalkenoate 9a. Triethylamine (0.6 mL) was added to a stirred solution of nosyloxy keto ester **8a** (690 mg, 1.7 mmol) in dichloromethane (20 mL). After being stirred at room temperature for 3 h, the mixture was diluted with dichloromethane (80 mL), washed with 1 N HCl (100 mL), passed through a short pad of $MgSO_4$ and silica gel 60, and evaporated to provide **9a** (160

(16) Prepared from (*S*)-methyl lactate (**7a**) or (*S*)-methyl 2-hydroxy-4-methylpentanoate (**7b**) by stirring with bromoacetyl chloride (1 equiv) in dichloromethane at room temperature overnight. Evaporation and bulb-to-bulb distillation (0.05 mmHg, 80–110 °C bath temperature) gave the bromoacetyl esters in quantitative yields.

mg, 47%) as a colorless oil after purification by radial chromatography (hexane/ethyl acetate (95:5 to 90:10)): $[\alpha]^{25}_D$ −11.14° (*c* 1.4, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 1.56 (d, *J* = 7.0 Hz, 3H, $CHCH_3$), 2.38 (s, 3H, $CH_3C(=O)$), 3.77 (s, 3H, OCH_3), 5.21 (q, *J* = 7.0 Hz, 1H, $CHCH_3$), 6.71 (d, *J* = 16.2 Hz, 1H, trans CH=CH), 7.08 (d, *J* = 16.2 Hz, 1H, trans CH=CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.07, 28.24, 52.69, 69.61, 130.54, 141.07, 164.81, 170.72, 197.43; IR (neat) 2998, 2956, 1731, 1686, 1453, 1362, 1260, 1216, 1175, 1099 cm^{-1}; Anal. Calcd for $C_9H_{12}O_5$: C, 54.00; H, 6.04. Found: C, 53.88; H, 5.99.

3-(Nosyloxy)-4-Keto Ester 8b. By the same three-step sequence *tert*-butyl acetoacetate was alkylated with bromo ester **7b**, reacted with pNBSP, and decarboxylated with TFA to give **8b** as a colorless oil in 48% yield after purification by flash chromatography (hexane/ethyl acetate (95:5 to 80:20)); ^1H NMR (200 MHz, $CDCl_3$) δ 0.91 (m, 6H, $CH(CH_3)_2$), 1.60–1.90 (m, 3H, $CH_2CH(CH_3)_2$), 2.37 (s, 3H, $CH_3C(=O)$), 2.95 (m, 2H, $CH_2C(=O)$), 3.72 and 3.70 (two s, 3H, OCH_3), 4.95 (m, 1H, $-OCHCO_2CH_3$), 5.21 (two dd, 1H, CHONs), 8.16 and 8.40 (AB q, 4H, aromatic H); IR (neat) 3108, 2959, 2873, 1743, 1608, 1535, 1352, 1187, 1014 cm^{-1}. This material was carried on without further characterization.

4-Oxoalkenoate 9b was prepared from **8b** in 68% yield by elimination using TEA as described above. The colorless oil had $[\alpha]^{25}_D$ −20.61° (*c* 1.1, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 0.96 (two d, *J* = 6.4 Hz, 6H, $CH(CH_3)_2$), 1.7–2.0 (m, 3H, $CH_2CH(CH_3)_2$), 2.39 (s, 3H, $CH_3C(=O)$), 3.77 (s, 3H, OCH_3), 5.16 (dd, *J* = 4.0, 11.2 Hz, 1H, $CHCO_2CH_3$), 6.73 (d, *J* = 16.2 Hz, 1H, trans CH=CH), 7.08 (d, *J* = 16.2 Hz, 1H, trans CH=CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.54, 22.98, 24.65, 28.11, 39.72, 52.42, 71.85, 130.51, 140.85, 164.97, 170.58, 197.36; IR (neat) 2959, 2873, 1731, 1692, 1643 cm^{-1}. Anal. Calcd for $C_{12}H_{18}O_5$: C, 59.49; H, 7.49. Found: C, 59.26; H, 7.53.

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