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Studies on the Reactivity of Methyl γ-Tosylcrotonoate as Ambident Reagent in Organic Synthesis

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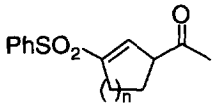
Abstract: The treatment of methyl (*E*)-4-tosyl-2-butenoate (**4**) with two equiv. of sodium hydride and different mono and dihalides gives mainly γ,γ- and α,α- or α,γ- and α,α-dialkylated products (**5-7**) depending on the electrophile. The corresponding monoanion dimerizes with iodine to afford stereoselectively dimethyl *cis*-4,5-ditosyl-2,6-cyclohexadiene-1,2-dicarboxylate (**11**). The tosyl group in compounds **6** and **7** is reduced and in the case of γ,γ-dimethylated **5a** substituted by sodium dimethyl malonate under $Pd(PPh_3)_4$ catalysis. Michael addition of different nucleophiles provides the corresponding β-substituted methyl γ-tosylbutanoates **16**. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

Substantial progress has been made in achieving γ-alkylation of dianions from α,β-unsaturated acids[1] and amides[2] specially crotonic acid derivatives, via their dianions. However, the alkylation of dienolate anions derived from 2-alkenoic esters takes place at the α-position to give the corresponding α-alkylated β,γ-unsaturated esters.[3] Even in the case of crotonic esters containing a methylthio[4] or a phenylsulfoxy[5a] group on the γ-carbon only α-alkylation is observed. The introduction of a more electron withdrawing group such as the phenylsulfonyl at the γ-position of methyl crotonoate **3** should direct the γ-alkylation such as has been demonstrated in the case of ketones **1**[5] and amide **2**.[6] Fifteen years ago, Lansbury *et al.*[5a] reported that the monodeprotonation of methyl γ-(phenylsulfonyl)crotonoate (**3**) with one equiv. of sodium hydride followed by alkylation with methyl iodide gave reasonable yields of the γ,γ-dimethylated product. Our interest in anions derived from functionalized sulfones of the type **2**[6] prompted us to study more extensively the reactivity of the homologous methyl γ-tosylcrotonoate (**4**) as nucleophile in alkylation reactions and also as electrophile in Michael type additions.



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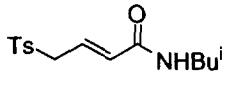

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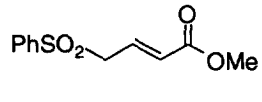

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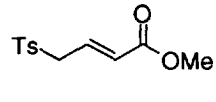
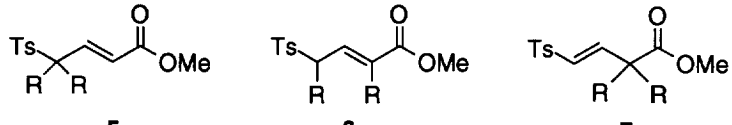


4

RESULTS AND DISCUSSION

The starting methyl γ-tosylcrotonoate (**4**) was prepared by nucleophilic substitution of commercially available methyl γ-bromocrotonoate with sodium *p*-toluenesulfinate in methanol in 90% yield. Initially we

studied the reaction of ester **4** with sodium hydride[7] in DMF or THF under different ester/base stoichiometry and with methyl iodide as electrophile. Under the conditions to prepare the monoanion intermediate the same ratio of γ,γ- and α,γ-dimethylated products **5a** and **6a** were obtained (Table 1, entry 1). Dimethylation took also place under dianion stoichiometry in DMF or THF to give γ,γ-dimethylated **5a** but also α,γ,γ- and α,α,γ-trimethylated compounds **8a** and **9a**, respectively (Table 1, entries 2 and 3). When the same dialkylation reaction was carried out at -78°C mainly dimethylated **5a** and **6a** together with trimethylated compounds **8a** and **9a** were obtained (Table 1, entry 4). These preliminary assays showed that polyalkylation was favoured independently of the number of equiv. of base or the reaction temperature. We never observed the predominant formation of compound **5a** as it has been previously reported for compound **3**.[5a]



5 **6** **7**

8 **9**

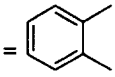
a: R = Me
b: R = $CH_2C{\equiv}CH$
c: R = $CH_2CH{=}CH_2$
d: R = Bu^n
e: R = $PhCH_2$
f: R-R = $(CH_2)_3$
g: R-R = 

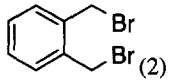
Table 1. Methylation of Methyl γ-Tosylcrotonoate (**4**).

	reaction conditions[a]			
entry	solvent	NaH (equiv)	MeI (equiv)	products (yield %)[b] ratio[c]
1	DMF	1	1	**5a: 6a** (38) 1: 1
2	DMF	2	2	**5a** (26)
				8a: 9a (29) 1.5: 1
3	THF	2	2	**5a** (22)
				8a: 9a (20) 1: 1
4	THF[d]	2	2	**5a: 6a** (62)[e] 4.5: 3
				8a: 9a (19)[e] 1.5: 1

[a] The reaction was carried out at room temperature for 1 d. [b] Based on ester **4**, after column chromatography on silica gel. [c] Determined on the crude reaction mixture by ^1H NMR (300 MHz). [d] The reaction was carried out at -78° to 0°C for 2 h. [e] Isolated crude yields.

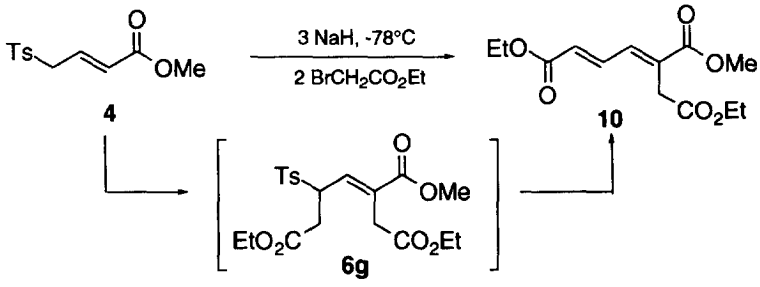
From the foregoing results we studied the alkylation with different alkyl halides under dianion stoichiometry. When compound **4** was treated with 2 equiv of sodium hydride in THF at room temperature for 1d and alkyl halides such as allyl or benzyl bromide, α,γ-dialkylated product **6** was mainly obtained, the α,α-compound **7** being the minor isomer (Table 2, entries 2 and 4). Butyl iodide also gave the same dialkylated products **6d** and **7d** (Table 2, entry 3). The less steric demanding propargyl bromide afforded γ,γ- and α,α-dialkylated products **5b** and **7b**, respectively. The use of α,α'-dibromo-*o*-xylene as dielectrophile gave cyclic γ,γ- and α,α- dialkylated products **5** and **7** (Table 2, entry 6). An excess of 4 equiv. of NaH and 3 equiv. of benzyl bromide provided only the α,α,γ-tribenzylated product **9e** (Table 2, entry 5). The assignment of the double bond configuration of compounds **5-9** was made by means of ^{1}H NMR studies on the basis of chemical shifts, coupling constants, or NOE difference experiments.

Table 2. Alkylation of Methyl γ-Tosylcrotonoate (**4**).

entry	RHal (equiv)	products (yield %)[a]	ratio[b]
1	$HC{\equiv}CCH_2Br$ (2)	**5b** (22): **7b** (25)	2: 1
2	$CH_2{=}CHCH_2Br$ (2)	**6c**: **7c** (70)	2.5: 1
3	Bu^nI (2)	**6d**: **7d** (20)[c]	2.5: 1
4	$PhCH_2Br$ (2)	**6e** (61): **7e** (9)	7: 1
5	$PhCH_2Br$ (3)[d]	**9e** (51)	
6	 (2)	**5f**: **7f** (51)	1: 1

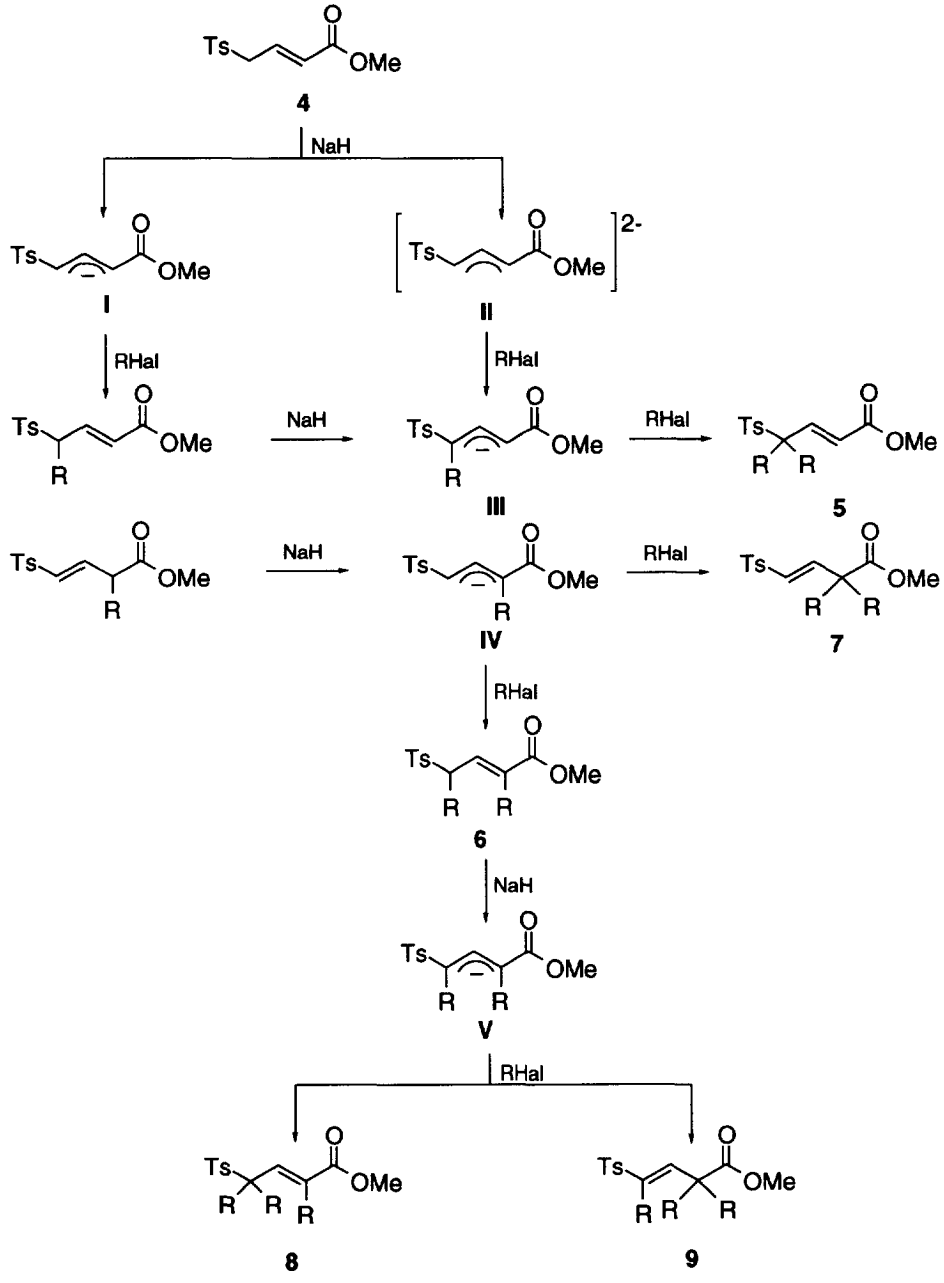
[a] Based on ester **4**, after column chromatography on silica gel. [b] Determined on the crude reaction mixture by ^{1}H NMR (300 MHz). [c] Less than 10% of trialkylated products **8d** and **9d** were also obtained. [d] 4 equiv. of NaH were used.

When the reaction with ethyl bromoacetate was performed using an excess of sodium hydride (3 equiv.) at -78°C the corresponding *in situ* dehydrosulfinylation was also achieved. Thus, the expected dienic triester **10** was regio and stereoselectively obtained in 43% yield, probably being the α,γ-dialkylated compound **6g** the intermediate (Scheme 1). The stereochemistry of the 1,6-diester **10** was stablished by NOE difference experiments.



Scheme 1.

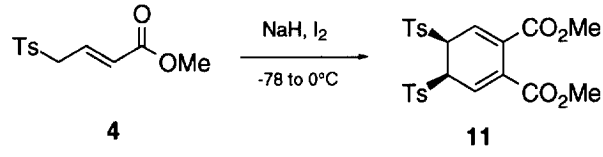
The regio and stereochemical results obtained in dialkylation reactions of compound **4** could be understood by participation of monoanions **III** and **IV** with *exo*-structures[8] formed either by monoalkylation of the dianion **II** or by subsequent alkylation-deprotonation of monoanion **I**. Dialkylated compounds **5**, **6**, and **7** derived from monoanions **III** and **IV**. Trialkylated derivatives **8** and **9** are probably formed by alkylation of anion **V** derived from compound **6** (Scheme 2).



Scheme 2.

The observed regioselectivity seems to be based on steric factors during the substitution process as it has been postulated for ketones **1**.[5] When α,γ-dialkylated compounds **6** are mainly formed, it means that once monoalkylation takes place to give anions **III** and **IV**, the most favoured process is the α and the γ-alkylation at the unsubstituted position, respectively. That happens with more hindered alkyl halides such as butyl, allyl, or benzyl halides and ethyl bromoacetate. For the less hindered electrophiles the second alkylation of monoanions **III** and **IV** occurs at the same position than the first one due to the greater reactivity of the more substituted anion to give mixtures of compounds **5** and **7**.

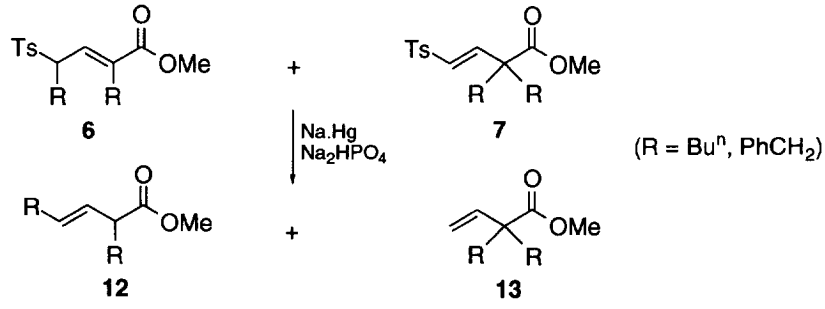
Dimerization of starting ester **4** was achieved by treatment with one equiv. of sodium hydride and iodine between -78 and 0°C for 2.5 h to afford regio and steroselectively the *cis*-derivative **11** as the only product in 49% and the starting ester being recovered in 27% yield (Scheme 3).



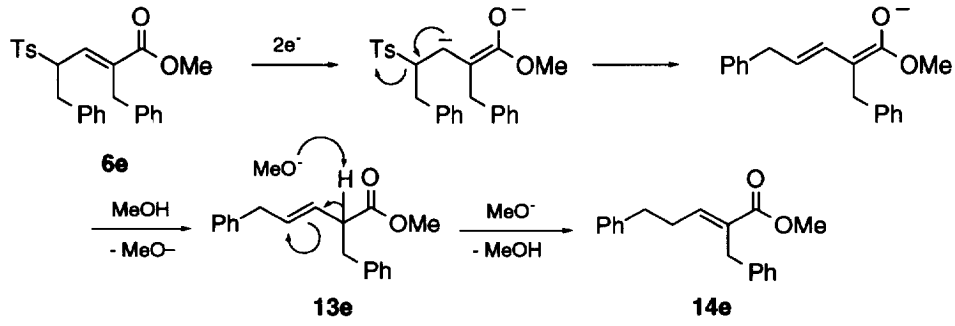
4 **11**

Scheme 3.

Reductive desulfonylation of dialkylated products **6** and **7** has been carried out with sodium amalgam in methanol buffered by Na_2HPO_4[9] for 1 h at room temperature to afford the corresponding desulfonylated compounds **12** and **13**, respectively in almost quantitative yields (Scheme 4). Deconjugated compounds **12** are formed due to the formation of the corresponding dienolates, which under the methanolic reduction conditions suffered kinetic protonation at the α-position of the ester.[10] However, when compound **6e** was reduced for longer time (2.5 h) the conjugated compound **14e** was almost exclusively obtained in 80% yield, as a consequence of the isomerization of the initially formed product **12e** to the thermodynamically more stable **14e** (Scheme 5).

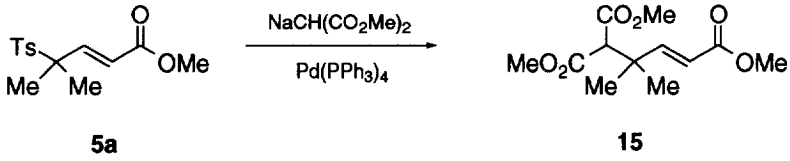


Scheme 4.



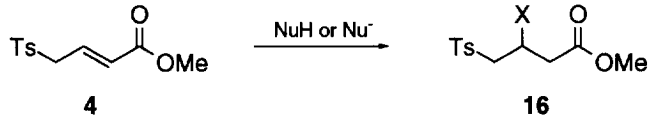
Scheme 5.

The application of Trost's methodology to create quaternary carbon centers[11] to the γ,γ-dimethylated sulfone **5a** by tetrakis(triphenylphosphine)palladium(0) catalysed substitution of the sulfone group by the sodium salt of dimethyl malonate under refluxing THF for 1 d afforded compound **15** in 60% yield (Scheme 6).



Scheme 6.

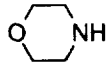
Conjugate addition of different nucleophiles to methyl γ-tosylcrotonoate (**4**) have also been studied in order to prepare 3-substituted methyl 4-tosylbutanoates[12] **16** (Scheme 7 and Table 3). In general all attempted nucleophiles reacted sluggishly with compound **4** except the lithium enolate derived from the benzophenone imine of glycine ethyl ester[13] which provided stereoselectively compound **16f** the protected glutamic acid derivative **16f** at low temperature. Compounds **16c** and **16e** were obtained as a mixture of *syn/anti* diastereomers which stereochemistry could not be assigned due to similar coupling constants (^{1}H NMR, see experimental) and conformational energies (molecular mechanics calculations).



Scheme 7.

In summary, methyl γ-tosylcrotonoate (**4**) is a crotonoic acid derivative which dianion shows a predominant tendency to suffer dialkylation at the α,γ-positions in the case of more substituted alkyl halides and at the α,α- and γ,γ-positions for less hindered ones. It also reacts at the β-position as electrophile with different nucleophiles to give the corresponding Michael addition products.

Table 3. Michael Addition of Nucleophiles to Methyl γ-Tosylcrotonoate (**4**).

	reaction conditions			product		
Nu (equiv)	solvent	time	temperature	no.	X	yield (%)[a]
 (10)	THF	8 d	reflux	**16a**		90
CH_3NO_2[b]	CH_3NO_2	3 h	rt	**16b**	O_2NCH_2	85
$O_2NCH_2CO_2Et$ (1.5)[b]	THF	3 d	rt	**16c**[c]	$O_2NCH(CO_2Et)$	42
$CH_2(CO_2Me)_2$ (1.5)[d]	THF	3 d	rt	**16d**	$CH(CO_2Me)_2$	43
$AcCH_2CO_2Me$ (1.5)[d]	THF	7 d	rt	**16e**[c]	$AcCH(CO_2Me)$	35
$EtO_2CCH_2N{=}CPh_2$ (1)[e]	THF	4 h	-78 to -40°C	**16f**[f]	$EtO_2CCH(N{=}CPh_2)$	54

[a] Based on ester **4**, after column chromatography (silica gel). [b] DBU (1.5 equiv) was used as base. [c] Mixture of *ca.*1:1 diastereomers. [d] NaH was used as the base. [e] LHMDS was used as the base. [f] Only one diastereomer.

EXPERIMENTAL SECTION

General. Melting points were obtained with a Reichert Thermovar apparatus and are uncorreted. FT-IR spectra were obtained on a Nicolet Impact 400D spectrophotometer as neat liquids. NMR spectra were recorded on a Brucker AC-300 (300 MHz for ^1H and 75 MHz for ^{13}C) using $CDCl_3$ as solvent and TMS as internal standard; chemical shifts are given in δ (ppm) and coupling constants (*J*) are measured in Hz. ^{13}C NMR assignements were made on the basis of DEPT experiments. Mass spectra (EI, 70 eV) were obtained on a Hewlett-Packard 5988A spectrometer. High resolution mass spectra were measured in the Mass Spectrometry Service at the University of Zaragoza. Elemental analyses were performed by the Microanalyses Service at the University of Alicante. Thin layer chromatography (TLC) was carried out on Schleicher & Schuell F1400/LS 254 plates coated with a 0.2 mm layer of silica gel and UV visualization. Column chromatography was performed using silica gel 60 of 70-230 mesh (hexane/ether). All starting materials were commercially available (Aldrich, Fluka, Across) of the best grade and were used without further purification. THF was dried over benzophenone ketyl under an argon atmosphere and distilled before use.

Synthesis of Methyl γ-Tosylcrotonoate (4): A solution of methyl 4-bromocrotonoate (0.895 g, 5 mmol) and sodium *p*-toluenesulfinate (1.75 g, 7 mmol) in methanol (10 mL) was stirred for 1 d at room temperature. Then, the solvent was removed in vacuo (15 Torr) and the resulting residue was dissolved in a mixture of ether (20 mL) and water (10 mL). The organic layer was decanted and aqueous phase was extracted with ether (2x20 mL). The organic layers were dried (Na_2SO_4) and evaporated (15 Torr) and the resulting residue was purified by column chromatography on silica gel to afford 1.135 g of pure ester **4** (90% yield) which was recrystallized and isolated as white crystalls: mp 52-53°C (hexane/ether); ν 3020, 1650, 975 (C=CH), 1715 (C=O), 1330, and 1150 cm^{-1} (SO_2); δ_H 2.45 (s, 3H, CH_3Ar), 3.73 (s, 3H, OCH_3), 3.93 (d,

J=7.8, 2H, CH_2S), 5.88 (d, J=15.6, 1H, CHCO), 6.78 (dt, J=15.6, 7.8, 1H, SCH_2CH), 7.36, and 7.74 (2d, J=8.0, 4H, ArH); δ_C 21.51 (CH_3Ar), 51.75 (OCH_3), 59.01 (CH_2S), 128.78 133.27 (CH=CH), 128.18, 129.84, 135.12 145.18 (ArC), and 165.11 (C=O); m/z 254 (M^+, 2%), 155 (34), 99 (15), 91 (100), 89 (12), 71 (13), 68 (92), 65 (29), 63 (11), and 41 (15) (Found: C, 56.08; H, 5.75; S, 12.31. Calcd. for $C_{12}H_{14}O_4S$: C, 56.68; H, 5.55; S, 12.61).

Metallation of Methyl (*E*)-4-Tosyl-2-butenoate (4). Reaction with Alkyl Halides. General Procedure. To a suspension of sodium hydride (16 mg, 0.66 mmol) in THF (2 mL) was added a solution of ester **4** (76 mg, 0.3 mmol) in THF (2 mL) and the resulting mixture was stirred for 1 h at room temperature and under argon. Then, the corresponding alkylating agent (0.66 mmol) was added and the reaction mixture was stirred for 24 h. The reaction was hydrolyzed with water and ether was added. The organic layer was washed with brine, dried (Na_2SO_4) and evaporated (15 Torr). The resulting residue was purified by column chromatography on silica gel to afford compounds **5-9**. Yields are included in Table 1 and 2, physical, spectral and analytical data follow.

***Methyl (E)-4-Methyl-4-tosyl-2-pentenoate* (5a):** R_f 0.66 (hexane/EtOAc: 1/1); ν 3000, 1650, 990 (C=CH), 1720 (C=O), 1330, and 1160 cm^{-1} (SO_2); δ_H 1.40 (s, 6H, 2xCH_3), 2.36 (s, 3H, CH_3Ar), 3.68 (s, 3H, OCH_3), 5.70, 6.95 (2d, J=15.9, 2H, CH=CH), 7.24, and 7.59 (2d, J=8.1, 4H, ArH); δ_C 20.53 (2xCH_3), 21.53 (CH_3Ar), 51.79 (OCH_3), 64.14 (CS), 123.78, 145.47 (CH=CH), 129.29, 130.22, 131.76, 145.03 (ArC), and 165.74 (C=O); m/z 251 (M^+-OCH_3, 0.9%), 127 (100), 99 (18), 96 (13), 95 (30), 91 (48), 89 (13), 67 (61), 65 (47), 63 (10), 59 (15), 53 (18), and 41 (30).

***Methyl (E)-2-Methyl-4-tosyl-2-pentenoate* (6a):** (impurified by **5a**) R_f 0.66 (hexane/EtOAc: 1/1);[14] ν 3020, 1650, 980 (C=CH), 1720 (C=O), 1330, and 1150 cm^{-1} (SO_2);[14] δ_H 1.52 (d, J=6.7, 3H, CH_3CHS), 1.55 (s, 3H, CH_3C), 2.44 (s, 3H, CH_3Ar), 3.74 (s, 3H, OCH_3), 3.96 (dq, J=10.7, 6.7, 1H, CHS), 6.48 (d, J=10.7, 1H, CH=C), 7.32, and 7.70 (2d, J=8.1, 4H, ArH); δ_C 12.67, 13.58 (2xCH_3), 21.53 (CH_3Ar), 52.06 (OCH_3), 60.00 (CHS), 133.42, 134.02 (CH=C), 128.95, 129.62, 133.63, 144.93 (ArC), and 167.13 (C=O); m/z 127 (M^+-Ts, 100%), 99 (18), 96 (13), 95 (30), 91 (48), 89 (13), 67 (61), 65 (47), 63 (10), 59 (15), 53 (18), and 41 (30).[14]

***Methyl (E)-2,4-Dimethyl-4-tosyl-2-pentenoate (8a) and Methyl (E)-2,2-Dimethyl-4-tosyl-3-pentenoate* (9a):** R_f 0.65 (hexane/ether: 1/4);[14] ν 3020, 1640, 995 (C=CH), 1710 (C=O), 1300, and 1150 cm^{-1} (SO_2);[14] δ_H 1.41 [s, 2.4H, $(CH_3)_2CCO$], 1.61 [s, 3.6H, $(CH_3)_2CS$], 1.73 [d, J=1.4, 1.2H, $CH_3(S)C$=CH], 1.82 [d, J=1.5, 1.8H, $CH_3(CO)C$=CH], 2.44, 2.45 (2s, 3H, CH_3Ar), 3.66 (s, 1.2H, $CHCCO_2CH_3$), 3.76 (s, 1.8H, CH=CCO_2CH_3), 6.70 (q, J=1.5, 0.6H, CH=CCO), 6.93 (q, J=1.4, 0.4H, CHCCO), 7.33, and 7.71 (2d, J=8.1, 4H, ArH); δ_C 11.77 [$CH_3(S)C$=CH], 13.38 [$CH_3(CO)C$=CH], 21.53, 21.58 (2xCH_3Ar), 22.85 [$(CH_3)_2CS$], 26.03 [$(CH_3)_2CCO$], 43.24 (CHCCO), 52.29 (CH=CCO_2CH_3), 52.33 ($CHCO_2CH_3$), 64.80 [$(CH_3)_2CS$], 137.64, 137.99, 143.53 (CH=CCO, SC=CH), 127.96, 129.37, 129.74, 130.38, 132.46, 133.22, 144.15, 144.89 (ArC), 168.40, and 175.72 (2xC=O); m/z 265 (M^+-OCH_3, 0.4%), 141 (100), 139 (13), 109 (52), 91 (11), 81 (29), and 67 (11).[14]

***Methyl (E)-4-Propargyl-4-tosyl-2-hepten-6-ynoate* (5b):** (impurified by **7b**) R_f 0.55 (hexane/ether: 1/4);[14] ν 3280, 2100 (C≡CH), 1730 (C=O), 1305, and 1150 cm^{-1} (SO_2);[14] δ_H 2.08 (t, J=2.6, 2H, 2xHC≡C), 2.45 (s, 3H, CH_3Ar), 2.91, 3.04 (2dd, J=17.3, 2.6, 4H, 2xCH_2), 3.78 (s, 3H, OCH_3), 5.96, 6.94 (2d, J=16.2, 2H, CH=CH), 7.34, and 7.72 (2d, J=8.5, 4H, ArH); δ_C 21.67 (CH_3Ar), 29.65 (2xCH_2), 52.01 (OCH_3), 67.53 (CS), 73.16 (2xHC≡C), 76.81 (2xHC≡C), 126.45, 140.78 (CH=CH), 129.59, 130.60, 131.88, 145.91 (ArC),

and 170.82 (C=O); *m/z* 329 (M^+-1, 2%), 175 (21), 139 (38), 116 (17), 115 (80), 92 (14), 91 (100), 89 (31), 77 (23), 71 (43), 69 (11), 65 (69), 63 (33), 59 (41), 57 (11), 55 (14), 51 (27), 50 (13), 43 (28), and 41 (21).[14]

***Methyl 2-Propargyl-2-[(E)-tosylvinyl]-4-pentynoate* (7b):** R_f 0.58 (hexane/ether: 1/4); ν 3280, 2120 (C≡CH), 3050, 1620, 970 (C=CH), 1730 (C=O), 1300, and 1140 cm^{-1} (SO_2); δ_H 2.02 (t, *J*=2.6, 2H, 2xHC≡C), 2.44 (s, 3H, CH_3Ar), 2.75, 2.83 (2dd, *J*=16.9, 2.6, 4H, 2xCH_2), 3.77 (s, 3H, OCH_3), 6.52, 7.03 (2d, *J*=15.6, 2H, CH=CH), 7.33, and 7.76 (2d, *J*=8.1, 4H, ArH); δ_C 21.62 (CH_3Ar), 24.97 (2xCH_2), 50.96 (*C*CO), 53.16 (OCH_3), 72.4 (HC≡*C*), 78.12 (*H*C≡C), 132.74, 142.77 (CH=CH), 127.83, 129.90, 136.90, 144.64 (ArC), and 170.82 (C=O); *m/z* 329 (M^+-1, 1%), 175 (30), 152 (10), 143 (11), 139 (59), 116 (25), 115 (83), 103 (15), 92 (18), 91 (100), 89 (35), 78 (13), 77 (36), 65 (65), 64 (12), 63 (39), 59 (71), 53 (12), 51 (45), 50 (18), 45 (11), and 41 (16).

***Methyl (E)-2-Allyl-4-tosyl-2,6-heptadienoate* (6c) *and Methyl 2-Allyl-2-[(E)-tosylvinyl]-4-pentenoate* (7c):** R_f 0.70 (hexane/ether: 1/4);[14] ν 3075, 1635, 990 (C=CH), 1715 (C=O), 1300, and 1145 cm^{-1} (SO_2);[14] δ_H 2.44-2.47 (m with s at 2.44, 3.7H, CH_3Ar, *H*CHC=CH), 2.54 (dd, *J*=14.7, 7.0, 0.7H, HC*H*C=CH), 2.70 [dd, *J*=15.6, 6.3, 0.6H, (*H*CH)$_2$CCH], 2.80 [dd, *J*=15.6, 6.0, 0.6H, (HC*H*)$_2$CCH], 2.94 (m, 1.4H, CH_2CHS), 3.70 (s, 0.9H, CHCCO$_2C_{H_3}$), 3.75 (s, 2.1H, CH=CCO$_2C_{H_3}$). 3.94 (td, *J*=10.8, 3.4, 0.7H, C*H*SCH), 4.78-4.86 [m, 1.2H, C(CH$_2$CH=C*H*$_2$)$_2$], 4.94-5.18 (m, 2.8H, CHSCH$_2$CH=C*H*$_2$, CH=CCH$_2$CH=C*H*$_2$), 5.37-5.74 [m, 2H, CHSCH$_2$C*H*=CH$_2$, CH=CCH$_2$C*H*=CH$_2$, C(CH$_2$C*H*=CH$_2$)$_2$], 6.44 (d, *J*=15.6, 0.3H, SC*H*=CH), 6.55 (d, *J*=10.8, 0.7H, CH=C), 7.04 (d, *J*=15.6, 0.3H, SCH=C*H*), 7.33, and 7.71 (2d, *J*=8.2, 4H, ArH); δ_C 21.48, 21.52 (2xCH_3Ar), 30.78, 32.37, 40.24 (*C*H$_2$CHS, *C*H$_2$C=CH, (*C*H$_2$)$_2$CCO), 51.76 (CH*C*CO), 52.09, 52.26 (2xOCH_3), 64.26 (S*C*HCH), 116.14, 118,90, 119,47, 127.57, 128.91 129.00, 129.25, 129.64, 129.77, 131.66, 131.76, 132.12, 133.38, 133.81, 134.21, 136.74, 145.07, 145.58 (ArC, olefinic signals), 166.46, and 172.44 (2xC=O); *m/z* 179 (M^+-Ts, 13%), 139 (13), 119 (38), 105 (13), 93 (10), 92 (15), 91 (100), 89 (13), 79 (22), 78 (10), 77 (32), 71 (11), 65 (45), 63 (13), 59 (22), 53 (11), 51 (14), and 41 (59).[14]

***Methyl (E)-2-Butyl-4-tosyl-2-octenoate* (6d), *and Methyl (E)-2,2-Dibutyl-4-tosyl-3-butenoate* (7d):** R_f 0.86 (hexane/ether: 1/4);[14] ν 1720 (C=O), 1302, and 1147 cm^{-1} (SO_2);[14] δ_H 0.77-1.03 {m, 6H, CH_3(CH$_2$)$_3$CHS, CH_3(CH$_2$)$_3$C=CH, [CH_3(CH$_2$)$_3$]$_2$C}, 1.05-1.34, 1.55-1.99, 2.20-2.25 {3m, 12H, CH_3(C*H*$_2$)$_3$CHS, CH_3(C*H*$_2$)$_3$C=CH, [CH_3(C*H*$_2$)$_3$]$_2$C}, 2.44 (s, 3H, CH_3Ar), 3.70 (s, 1.3H, CHCCO$_2C_{H_3}$), 3.75 (s, 1.7H, CH=CCO$_2C_{H_3}$), 3.81 (td, *J*=11.2, 3.5, 0.5H, SC*H*CH), 6.42 (d, *J*=11.2, 0.5H, CH=C), 6.45, 7.07 (2d, *J*=15.7, 0.7H, SCH=CH), 7.07 (d, *J*=15.7, 0.35H, SCH=C*H*), 7.32, 7.33, 7.70, and 7.75 (4d, *J*=8.2, 4H, ArH); δ_C 13.72, 13.76 {*C*H$_3$(CH$_2$)$_3$CHS, *C*H$_3$(CH$_2$)$_3$C=CH, [*C*H$_3$(CH$_2$)$_3$]$_2$C}, 21.58, 21.61 (2xCH_3Ar), 22.46, 22.70, 22.86, 26.62, 26.94, 27.42, 28.79, 30.80 {CH_3(*C*H$_2$)$_3$CHS, CH_3(*C*H$_2$)$_3$C=CH, [CH_3(*C*H$_2$)$_3$]$_2$C}, 37.02 (CH*C*CO), 52.04, 52.37 (2xOCH_3), 65.14 (S*C*HCH), 131.04, 137.62, 139.52, 147.35 (CH=CH, CH=C), 127.59, 129.12, 129.60, 129.87, 132.70, 134.66, 144.27, 144.91 (ArC), 167.11, and 173.77 (2xC=O); *m/z* 367 (M^++1, 0.1%), 212 (12), 211 (100), 179 (10), 151 (30), 139 (21), 109 (17), 95 (68), 93 (10), 91 (53), 81 (41), 79 (20), 77 (15), 71 (11), 69 (15), 67 (44), 65 (28), 59 (24), 55 (43), 53 (16), 45 (10), 43 (21), and 41 (49).[14]

***Methyl (E)-2-Benzyl-5-phenyl-4-tosyl-2-pentenoate* (6e):** mp 104-105°C (hexane/ether); ν 3050, 3020, 1640, 1590, 970 (C=CH), 1715 (C=O), 1295, and 1145 cm^{-1} (SO_2); δ_H 2.46 (s, 3H, CH_3Ar), 2.82, 2.94 (2d, *J*=15.2, 2H, CH_2C), 2.96 (dd, *J*=13.6, 11.4, 1H, *H*CHCH), 3.63 (s, 3H, OCH_3), 3.64 (dd, *J*=13.6, 2.8, 1H, HC*H*CH), 4.10 (td, *J*=11.4, 2.8, 1H, CHS), 6.30 (d, *J*=7.3, 2H, ArH), 6.75 (d, *J*=11.4, 1H, CH=C), 6.90-7.26 (m, 8H, ArH), 7.33, and 7.74 (2d, *J*=8.4, 4H, ArH); δ_C 21.66 (CH_3Ar), 31.96, 34.26 (*C*H$_2$CHS, *C*H$_2$C), 52.09 (OCH_3), 66.79 (CHS), 125.87, 127.07, 127.73, 128.14, 128.78, 129.05, 129.33, 129.83, 133.15, 134.25,

135.81, 137.43, 138.10, 145.17 (CH=C, ArC), and 166.39 (C=O); *m/z* 403 (M^+-OCH_3, 0.3 %), 279 (22), 278 (27), 247 (14), 219 (13), 187 (32), 141 (13), 128 (13), 115 (17), 92 (11), and 91 (100).

***Methyl (E)-2,2-Dibenzyl-4-tosyl-3-butenoate* (7e):** (impurified by **6e**) R_f 0.63 (hexane/EtOAc: 1/1);[14] ν 1715 (C=O), 1295, and 1145 cm^{-1} (SO_2);[14] δ_H 2.44 (s, 3H CH_3Ar), 2.98, 3.33 (2d, *J*=13.7, 4H, CH_2C), 3.63 (s, 3H OCH_3), 6.43 (d, *J*=15.7, 1H, CHS), 6.93-7.29 (m, 13H, SCH=C*H*, ArH), and 7.61 (d, *J*=8.3, 2H, ArH); δ_C 21.57 (CH_3Ar), 44.67 (2xCH_2), 52.00 (OCH_3), 54.82 (*C*CO), and 172.36 (C=O);[15] *m/z* 403 (M^+-OCH_3, 0.3 %), 279 (22), 278 (27), 247 (14), 219 (13), 187 (32), 141 (13), 128 (13), 115 (17), 92 (11), and 91 (100).[14]

***Methyl (E)-2,2-Dibenzyl-5-phenyl-4-tosyl-3-pentenoate* (9e):** mp 147-148°C (hexane/ether); ν 3061, 3028, 1595 (C=CH), 1737 (C=O), 1300, and 1145 cm^{-1} (SO_2); δ_H 2.36 (s, 3H, CH_3Ar), 3.08 (s, 2H, CH_2CS), 3.09, 3.21 (2d, *J*=13.7, 4H, CH_2CCO), 3.31 (s, 3H, OCH_3), 6.82, 6.98, 7.09, 7.24 (4m, 18H, C=CH, ArH), and 7.35 (d, *J*=8.2, 2H, ArH); δ_C 21.46 (CH_3Ar), 32.58 (CH_2CS), 44.04 (2xCH_2CCO), 51.68 (OCH_3), 54.23 (*C*CO), 126.12, 127.00, 127.82, 128,09, 128,21, 128.97, 129.25, 130,41, 135.48, 135.87, 137.17, 142.79, 143.34, 143.56 (C=CH, ArC), and 172.97 (C=O); *m/z* 369 (M^+-Ts, 0.6%), 278 (13), 277 (52), 92 (11), 91 (100), and 65 (13) (Found: C, 73.96; H, 6.19; S, 5.88. Calcd. for $C_{33}H_{32}O_4S$: C, 75.54; H, 6.15; S, 6.11).

***2-[(E)-Methoxycarbonylvinyl]-2-tosylindane* (5f) *and 2-(Methoxycarbonyl)-2-[(E)-tosylvinyl]indane* (7f):** R_f 0.50 (hexane/ether: 1/4);[14] ν 3050, 1600, 915 (C=CH), 1730 (C=O), 1300, and 1145 cm^{-1} (SO_2);[14] δ_H 2.41, 2.43 (2s, 3H, CH_3Ar), 3.06, 3.91 [2d, *J*=16.2, 1.8H, $(CH_2)_2CS$], 3.08, 3.61 [2d, *J*=16.0, 2.2H, $(CH_2)_2CCO$], 3.68 (s, 1.35H, $CHCO_2CH_3$), 3.72 (s, 1.65H, CCO_2CH_3), 5.76 (d, *J*=16.2, 0.45H, CHCO), 6.30, 7.20 (2d, *J*=15.3, 1.1H, SCH=CH), 7.13 (m, 4.45H, 8H of ArH, *CH*=CHCO), 7.29, 7.66 (2d, *J*=8.5, 2.2H, 4H of ArH), 7.32, and 7.72 (2d, *J*=8.4, 1.8H, 4H of ArH); δ_C 21.51, 21.57 (2xCH_3Ar), 38.88 [$(CH_2)_2CS$], 41.94 [$(CH_2)_2CCO$], 51.79 ($CHCO_2CH_3$), 52.83 (CCO_2CH_3), 55.71 (*C*CO), 73.93 (CS), 124.32, 124.34, 127.13, 127.31, 127.50, 129.56, 129.76, 129.84, 130.21, 133.18, 137.07, 138.25, 139.35, 143.76, 144.39, 145.23 and 146.16 (*C*H=*C*HCO, SCH=CH, ArC), 165.64, and 173.39 (2xC=O); *m/z* 325 (M^+-OCH_3, 0.3%), 201 (23), 200 (16), 169 (19), 168 (26), 142 (24), 141 (100), 140 (26), 139 (26), 129 (14), 128 (16), 116 (14), 115 (96), 92 (12), 91 (90), 89 (23), 77 (11), 65 (70), 63 (28), 59 (24), 55 (11), 51 (14), and 45 (13).[14]

***Diethyl (2E, 4E)-5-(Methoxycarbonyl)hepta-2,4-diendioate* (10):** R_f 0.72 (hexane/ether: 1/4); ν 1605, 975 (C=CH), 1710 cm^{-1} (C=O); δ_H 1.26, 1.32 (2t, *J*=7.2, 6H, 2xCH_2CH_3), 3.55 (s, 2H, CH_2CO), 3.81 (s, 3H, OCH_3), 4.16, 4.25 (2q, *J*=7.2, 4H, 2xOCH_2), 6.23 (d, *J*=14.3, 1H, CHCO), 7.38 (d, *J*=11.9, 1H, CH=C), and 7.47 (dd, *J*=14.3, 11.9, 1H, CH=C*H*CH); δ_C 14.10, 14.21 (2xCH_2CH_3), 32.86 (CH_2CO), 52.42 (OCH_3), 60.90, 61.19 (2xOCH_2), 128.99 131.39, 137.25, 137.31 (CH=CHCH=C), 165.95, 166.86, and 169.79 (3xC=O); *m/z* 270 (M^+, 1%), 238 (14), 225 (28), 212 (13), 211 (100), 210 (24), 197 (78), 183 (32), 169 (14), 165 (12), 155 (14), 151 (10), 149 (20), 138 (13), 137 (37), 125 (12), 124 (29), 123 (10), 121 (18), 111 (12), 110 (25), 109 (34), 95 (21), 94 (24), 93 (57), 92 (13), 91 (12), 82 (26), 81 (25), 79 (30), 77 (14), 69 (20), 66 (33), 65 (75), 64 (14), 63 (27), 59 (82), 57 (15), 55 (23), 53 (37), 45 (35), 43 (54), and 41 (31) (Found: M^+ 270.1112. Calcd. for $C_{13}H_{18}O_6$: 270.1103).

***Dimethyl* cis-*4,5-Ditosyl-2,6-cyclohexadien-1,2-dicarboxylate* (11):** mp 172-173°C (hexane/ether); ν 1738 (C=O), 1326, and 1151 cm^{-1} (SO_2); δ_H 2.46 (s, 6H, 2xCH_3Ar), 3.73 (s, 6H, 2xOCH_3), 3.94 (m, 2H, 2xCHS), 7.23 (m, 2H, 2xCH=C), 7.38, and 7.78 (2d, *J*=8.1, 8H, ArH); δ_C 21.75 (2xCH_3Ar), 53.04 (2xCHS), 53.21 (2xOCH_3), 109.50 (2x*C*CO), 129.37, 130.05, 133.18, 145.48 (ArC), 142.18 (2x*C*H=C), and 168.57 (2xC=O); *m/z* 503 (M^+-1, 0.7%), 289 (16), 254 (10), 195 (23), 193 (10), 163 (26), 155 (18), 139 (90), 128 (14),

127 (16), 92 (21), 91 (100), 77 (19), 65 (33), 62 (11), and 58 (19) (Found: C, 56.58; H, 5.10; S, 12.69. Calcd for $C_{24}H_{24}O_8S_2$: C, 57.13; H, 4.79; S, 12.71).

Reduction of Compounds 6 and 7 with Sodium Amalgam. General Procedure. To a suspension of Na_2HPO_4 (87 mg, 0.61 mmol), and ca. 6 % sodium amalgam (583 mg, 1.5 mmol) in dry methanol (4 mL) was dropped at 0° C a solution of the corresponding sulphone **6** and **7** (0.15 mmol) in methanol (1 mL). The reaction mixture was stirred at room temperature until the reduction was complete (monitored by TLC and GLC). Then, the reaction mixture was hydrolyzed with water and extracted with dichloromethane (3x15 mL). The organic layer was dried (Na_2SO_4), concentrated in vacuo (15 Torr) and the residue was purified by column chromatography to yield pure compounds **12** and **13** or **14e**. Yields are mentioned in the text, physical, spectroscopic and analytical data follow.

***Methyl (E)-2-Butyl-3-octenoate* (12d) *and Methyl (E)-2,2-Dibutyl-3-butenoate* (13d):** R_f 0.89 (hexane/ether: 1/4);[14] ν 1741 cm^{-1} (C=O);[14] δ_H 0.83-1.72 {m, 16.3H, $[CH_3(CH_2)_3]_2C$, $CH_3(CH_2)_3CHCO$, $CH_3(CH_2)_2CH_2CH{=}CH$}, 2.01 (m, 1.7H, $CH_2CH{=}CH$), 2.94 (m, 0.85H, CHCO), 3.67 (s, 2.55H, $CHCO_2CH_3$), 3.68 (s, 0.45H, CCO_2CH_3), 5.07 (d, *J*=17.8, 0.15H, *H*CH=CH), 5.16 (d, *J*=11.0, 0.15H, HC*H*=CH), 5.52 (dt, *J*=15.4, 6.5, 0.85H, $CH_2CH{=}CH$), and 5.99 (dd, *J*=17.8, 11.0, 0.15H, $CH_2{=}CHC$); δ_C 13.92, 14.04, 14.10, 22.13, 22.40, 22.69, 29.29, 29.70, 31.35, 31.93, 32.10, 32.34 {$[CH_3(CH_2)_3]_2C$, $CH_3(CH_2)_3CHCO$, $CH_3(CH_2)_3CH{=}CH$}, 35.88 (CCO), 38.74 (CHCO), 49.24 ($CHCO_2CH_3$), 51.60 (CCO_2CH_3), 127.64, 133.41 (CH=CH), 128.79, 130.86 (CH_2=CH), and 175.30 (2xC=O); *m/z* 212 (M^+, 1%), 185 (33), 181 (30), 169 (36), 155 (100), 153 (20), 129 (15), 128 (13), 121 (10), 116 (11), 115 (25), 98 (53), 83 (20), 59 (11), 57 (20), and 43 (10).[14]

***Methyl (E)-2-Benzyl-5-phenyl-3-pentenoate* (12e) *and Methyl (E)-2,2-Dibenzyl-3-butenoate* (13e):** R_f 0.82 (hexane/ether: 1/4);[14] ν 3020, 1640 (C=CH), and 1715 cm^{-1} (C=O);[14] δ_H 2.82 [dd, *J*=13.6, 7.8, 0.8H, *H*CHCHCO), 3.04, 3.22 [2d, *J*=13.7, 0.9H, $(CH_2)_2C$], 3.09 (dd, *J*=13.6, 7.5, 0.8H, HC*H*CHCO), 3.32 (m, 2.3H, $CH_2CH{=}CH$, CHCO), 3.62 (s, 0.7H, CCO_2CH_3), 3.63 (s, 2.3H, $CHCO_2CH_3$), 5.20 (d, *J*=17.8, 0.2H, *H*CH=CH), 5.30 (d, *J*=11.0, 0.2H, HC*H*=CH), 5.49-5.65 (m, 1.5H, CH=CH), 6.03 (dd, *J*=17.8, 11.0, 0.2H, CH_2=C*H*), 7.00-7.26 (m, 10H, ArH); δ_C 29.69 [$(CH_2)_2C$], 38.70, 43.76 ($CH_2CH{=}CH$, CH_2CHCO) 43,77 (CCO), 50.97, 51.77 (CHCO, $CHCO_2CH_3$), 51.67 (CCO_2CH_3), 115.76, 125.75, 126.01, 126.31, 126.46, 127.89, 128.31, 128.45, 128.80, 129.08, 130.27, 132.45, 137.12, 138.69, 139.06, 139.87 (CH=CH, CH_2=CH, ArC), 174.15, and 174.62 (2xC=O); *m/z* 280 (M^+, 15%), 248 (10), 191 (15), 189 (20), 163 (10), 157 (20), 143 (15), 129 (40), 117 (15), 115 (18), 104 (20), 91 (100), 77 (25), 65 (40), and 51 (10).[14]

***Methyl (E)-2-Benzyl-5-phenyl-2-pentenoate* (14e):** R_f 0.82 (hexane/ether: 1/4); ν 3061, 3027, 1645 (C=CH), and 1715 cm^{-1} (C=O); δ_H 2.59 (m, 2H, CH_2CH_2CH), 2.75 (m, 2H, CH_2CH_2CH), 3.64 (s, 2H, CH_2C), 3.68 (s, 3H, OCH_3), 6.99 (dd, *J*=15.0, 7.3, 1H, CH=C), and 7.09-7.31 (m, 10H, ArH); δ_C 30.89 (CH_2CH_2CH), 32.30 (CH_2CH_2CH), 34.78 (CH_2C), 51.77 (OCH_3), 125.95, 126.15, 128.14, 128.33, 128.47, 129.08, 131.37, 139.52, 140.92, 142.93 (CH=C, ArC), and 167.99 (C=O); *m/z* 280 (M^+, 25%), 248 (15), 189 (18), 157 (16), 143 (13), 129 (56), 128 (26), 121 (10), 117 (13), 116 (11), 115 (20), 105 (10), 104 (18), 92 (23), 91 (100), 77 (13), 65 (38), 59 (16), and 51 (14) (Found: M^+ 280.1463. Calcd. for $C_{19}H_{20}O_2$: 280.1463).

Synthesis of Dimethyl (E)-2-(Methoxycarbonyl)-3,3-dimethyl-4-hexenedioate (15). A solution of methyl (*E*)-4-methyl-4-tosyl-2-pentenoate **5a** (85 mg, 0.3 mmol) and tetrakis(triphenylphosphine) palladium (0) (70 mg, 0.06 mmol) in THF (2 mL) was stirred under argon during 45 min at room temperature. Then, this resulting mixture was added dropwise to a solution of sodium dimethyl malonate (0.48 mmol) in THF (2 mL)

and the reaction mixture was refluxed for 1 d. The cooled reaction mixture was hydrolyzed with water and extracted with ether (3x15 mL). The organic layer was dried (Na_2SO_4) and evaporated (15 Torr) to give a residue which was purified by column chromatography on silica gel to afford 46 mg of pure product **15** (60 % yield): R_f 0.63 (hexane/ether: 1/4); ν 3000, 1650, 870 (C=CH), 1755, and 1730 cm^{-1} (3xC=O); δ_H 1.28 (s, 6H, 2xCH_3C), 3.43 (s, 1H, COCHCO), 3.71 [s, 6H, C(CO_2CH_3)$_2$], 3.74 (s, 3H, CHCO$_2$CH_3), 5.82, 7.17 (2d, *J*=15.9, 2H, CH=CHCO); δ_C 25.01 (2x*C*H$_3$C), 38.62 (C), 51.57 (CHCO$_2$*C*H$_3$), 52.28 [C(CO_2CH_3)$_2$], 60.15 (CO*C*HCO), 118.91 (CH=*C*HCO), 154.18 (*C*H=CHCO), 167.09, and 167.79 (3xC=O); *m/z* 258 (M^+, 1.4%), 199 (21), 195 (20), 194 (27), 167 (17), 166 (12), 139 (39), 135 (43), 134 (10), 132 (11), 127 (100), 126 (40), 125 (11), 107 (10), 100 (13), 99 (17), 96 (11), 95 (65), 81 (16), 79 (25), 69 (28), 68 (11), 67 (62), 65 (17), 59 (59), 55 (19), 53 (25), 45 (10), 44 (19), 43 (19), 41 (61), and 40 (13) (Found: M^+ 258.1100. Calcd. for $C_{12}H_{18}O_6$: 258.1103).

Synthesis of Compounds 16. General Procedure. A solution of methyl (*E*)-4-tosyl-2-butenoate **4** (76 mg, 0.3 mmol) and nucleophile in the corresponding solvent (0.5-5 mL) (see Table 3) was stirred at the temperature and for the time shown in Table 3. The resulting mixture was hydrolyzed with water and extracted with ether (3x15 mL). In the case of compounds **16b** and **16c** the reaction mixture was dissolved in ether (15 mL) and washed with 2M HCl (2x15 mL). The organic layer was dried (Na_2SO_4) and evaporated (15 Torr) giving a residue which was purified by column chromatography on silica gel to afford products **16**. Yields are included in Table 3, physical, spectral and analytical data follow.

***Methyl 3-Morpholino-4-tosylbutanoate* (16a):** mp 96-97 °C (hexane/ether); ν 1733 (C=O), 1301, and 1147 cm^{-1} (SO_2); δ_H 2.23, 2.32 (2ddd, *J*=11.3, 6.1, 3.1, 4H, 2xCH_2N), 2.37 (s, 3H, CH_3Ar), 2.50 (d, *J*=6.7, 1H, *H*CHCO), 2.51 (d, *J*=7.3, 1H, HC*H*CO), 3.00 (dd, *J*=14.5, 7.0, 1H, *H*CHS), 3.29-3.42 (m with dd at 3.34, *J*=14.5, 6.1, 5H, HC*H*S, 2xCH_2O), 3.49 (m, 1H, CHN), 3.60 (s, 3H, OCH_3), 7.29, and 7.73 (2d, *J*=8.2, 4H, ArH); δ_C 21.37 (*C*H$_3$Ar), 34.86 (*C*H$_2$CO), 47.90 (2xCH_2N), 51.61 (OCH_3), 55.21 (CHN), 56.47 (CH_2S), 66.42 (2xCH_2O), 127.80, 129.60, 136.82, 144.47 (ArC), and 171.36 (C=O); *m/z* 341 (M^+, 3%), 268 (50), 185 (10), 172 (100), 128 (29), 126 (15), 113 (19), 91 (57), 86 (17), 68 (10), 65 (28), 59 (15), 56 (19), 55 (34), 54 (10), 42 (21), and 41 (16) (Found: C, 56.30; H, 6.93; N, 4.12; S, 8.41. Calcd. for $C_{16}H_{23}NO_5S$: C, 56.29; H, 6.79; N, 4.10; S, 9.39).

***Methyl 4-Nitro-3-(tosylmethyl)butanoate* (16b):** R_f 0.36 (hexane/ether: 1/4); ν 1725 (C=O), 1545, 1375 (NO_2), 1301, and 1147 cm^{-1} (SO_2); δ_H 2.46 (s, 3H, CH_3Ar), 2.67 (dd, *J*=17.6, 6.7, 1H, *H*CHCO), 2.75 (dd, *J*=17.6, 6.0, 1H, HC*H*CO), 3.13 (m, 1H, CH), 3.31 (dd, *J*=14.5, 5.8, 1H, *H*CHS), 3.37 (dd, *J*=14.5, 6.7, 1H, HC*H*S), 3.66 (s, 3H, OCH_3), 4.68 (dd, *J*=13.7, 6.4, 1H, *H*CHN), 4.81 (dd, *J*=13.7, 5.6, 1H, HC*H*N), 7.39, and 7.79 (2d, *J*=8.2, 4H, ArH); δ_C 21.52 (*C*H$_3$Ar), 29.26 (CH), 34,45 (*C*H$_2$CO), 51.93 (OCH_3), 55.89 (CH_2S), 76.40 (CH_2N), 127.83, 130.06, 135.69, 145.32 (ArC), and 170.81 (C=O); *m/z* 284 (M^+-OCH_3, 1.6%), 160 (35), 157 (11), 155 (18), 139 (23), 129 (16), 128 (11), 100 (44), 99 (13), 92 (16), 91 (100), 89 (14), 65 (42), 63 (12), 59 (33), 55 (26), 53 (11), 42 (16), and 41 (17).

***Methyl* syn/anti-*4-(Ethoxycarbonyl)-4-nitro-3-(tosylmethyl)butanoate* (16c):** R_f 0.42 (hexane/ether: 1/4); ν 1748 (C=O), 1564, 1318 (NO_2), 1305, and 1147 cm^{-1} (SO_2); δ_H 1.29, 1.31 (2t, *J*=7.2, 3H, CH_2CH_3), 2.47 (s, 3H, CH_3Ar), 2.72 (dd, *J*=17.9, 7.9, 1H, *H*CHCO of one diastereomer), 3.02 (dd, *J*=17.9, 5.2, 1H, HC*H*CO of one diastereomer), 2.79 (dd, *J*=18.0, 6.3, 1H, *H*CHCO of the other diastereomer), 2.90 (dd, J=18.0, 6.0, 1H, HC*H*CO of the other diastereomer), 3.29-3.47 (m, 3H, CH_2S, CH_2CHCH_2), 3.68, 3.69 (2s, 3H, OCH_3), 4.24, 4.30 (2q, *J*=7.2, 2H, CH_2CH$_3$), 5.78, 5.80 (2d, *J*=4.6, 1H, $CHNO_2$), 7.39, and 7.79 (2d,

J=8.4, 4H, ArH); δ_C 13.75, 13.77 (CH_2CH_3), 21.62 (CH_3Ar), 31.53, 31.66 (CH_2CHCH_2), 33.48, 33.59 (CH_2CO), 52.10 (OCH_3), 54.80, 55.29 (CH_2S), 63.45, 63.49 (CH_2CH_3), 87.23, 87.62 ($CHNO_2$), 128.05, 128.28, 129.92, 130.10, 135.52, 145.37 (ArC), 162.95, 163.01, 170.97, and 170.98 (2xC=O); *m/z* 232 (M^+-Ts, 19%), 202 (10), 157 (12), 155 (21), 139 (29), 129 (11), 128 (11), 113 (14), 99 (16), 97 (13), 92 (17), 91 (100), 89 (12), 85 (17), 71 (12), 65 (33), 59 (26), 57 (10), 55 (12), 53 (12), 43 (15), 42 (11), and 41 (15).

***Dimethyl 2-(Methoxycarbonyl)-3-(tosylmethyl)pentanedioate* (16d):** R_f 0.24 (hexane/ether: 1/4); ν 1754, 1732 (3xC=O), 1304, and 1163 cm^{-1} (SO_2); δ_H 2.46 (s, 3H, CH_3Ar), 2.71 (dd, *J*=17.1, 7.3, 1H, *H*CHCO), 2.89 (dd, *J*=17.1, 5.5, HC*H*CO), 3.01 (m, 1H, CH_2CHCH_2), 3.38 (dd, *J*=14.7, 7.3, 1H, *H*CHS), 3.47 (dd, *J*=14.7, 4.9, 1H, HC*H*S), 3.65, 3.66, 3.72 (3s, 9H, $3xOCH_3$), 4.01 (d, *J*=4,9, 1H, COCHCO), 7.38, and 7.79 (2d, *J*=8.2, 4H, ArH); δ_C 21.53 (CH_3Ar), 30.06 (CH_2CHCH_2), 34.78 (CH_2CO), 51.73, 52.26, 52.59 ($3xOCH_3$), 52.59 (*C*HCO), 56.17 (CH_2S), 128.02, 129.84, 135.94, 144.82 (ArC), 168.10, 168.11, and 171.61 (3xC=O); *m/z* 355 (M^+-OCH_3, 9%), 323 (32), 281 (14), 255 (17), 232 (14), 231 (100), 223 (14), 199 (83), 167 (79), 157 (31), 155 (24), 139 (53), 132 (10), 111 (10), 99 (18), 91 (56), 71 (10), 69 (12), 65 (22), and 59 (36).

***Dimethyl* syn/anti-*2-Acetyl-3-(tosylmethyl)pentanedioate* (16e):** R_f 0.35 (hexane/ether: 1/4); ν 1735, 1730 (C=O, 2xCO2), 1300, and 1150 cm^{-1} (SO_2); δ_H 2.20, 2.26 (2s, 3H, CH_3CO), 2.46 (s, 3H, CH_3Ar), 2.69, 3.02 (2m, 3H, CH_2CO, CH_2CHCH_2), 3.33-3.43 (m, 2H, CH_2S), 3.63, 3.67, 3.71 (3s, 6H, $2xOCH_3$), 4.14 (d, *J*=4.6, 1H, CHCO of one diastereomer), 4.24 (d, *J*=5.5, 1H, CHCO of the other diastereomer), 7.37, 7.76, and 7.78 (3d, *J*=8.4, 4H, ArH); δ_C 21.58 (CH_3Ar), 29.37, 29.68 (CH_2CHCH_2), 30.00, 30.22 (CH_3CO), 34.57 (CH_2CO), 51.74, 51.79, 52.52, 52.62 ($2xOCH_3$), 55.96, 56.05 (*C*HCO), 59.22, 59.36 (CH_2S), 127.94, 128.04, 129.91, 136.03, 136.27, 144.88, 144.90 (ArC) 168.62, 171.89, 172.03 ($2xCO_2$), 201.93, and 202.31 (C=O); *m/z* 370 (M^+, 1%), 307 (25), 223 (22), 215 (24), 190 (11), 183 (60), 164 (31), 157 (14), 155 (23), 154 (11), 151 (10), 141 (100), 140 (35), 139 (20), 132 (11), 112 (13), 109 (14), 99 (14), 91 (59), 65 (18), 59 (13), and 43 (69).

***Methyl 4-(Ethoxycarbonyl)-2-(diphenylmethylidenamino)-3-(tosylmethyl)butanoate* (16f):**[16] mp 141-142°C (hexane/ether); ν 1730, 1710 (2xC=O), 1620 (C=N), 1295, and 1136 cm^{-1} (SO_2); δ_H 1.18 (t, *J*=7.0, 3H, CH_3CH_2), 2.36 (s, 3H, CH_3Ar), 2.68 (dd, *J*=15.9, 7.3, 1H, *H*CHCO), 2.80 (m, 1H, CH_2CHCH_2), 2.94 (dd, *J*=15.9, 7.3, HC*H*CO), 3.31 (dd, *J*=14.6, 7.0, 1H, *H*CHS), 3.51 (s, 3H, OCH_3), 3.68 (dd, *J*=14.6, 4.6, 1H, HC*H*S), 4.07 (q, *J*=7.0, 2H, CH_3CH_2), 4.35 (d, *J*=4.0, 1H, CHN), 7.08, 7.24, 7.43, 7.52 (m, d, *J*=7.9, m, d, *J*=8.2, 10H, ArH), 7.32, and 7.76 (2d, *J*=7.5, 4H, ArH); δ_C 13.96 (CH_3CH_2), 21.46 (CH_3Ar), 34.73 ($CHCH_2S$), 34.83 (CH_2CO), 51.47 (OCH_3), 55.79 (CH_2O), 61.02 (CH_2S), 65.33 (CHN), 127.52, 127.86, 128.10, 128.36, 128.69, 128.72, 129.67, 130.58, 135.65, 135.87, 138.90, 144.44 (ArC), 170.15, 171.81 ($2xCO_2$), and 172.23 (C=N); *m/z* 521 (M^+, 3%), 448 (30), 292 (19), 283 (12), 266 (34), 265 (25), 232 (12), 219 (13), 193 (37), 192 (18), 166 (24), 165 (61), 139 (14), 129 (10), 115 (14), 105 (11), 92 (16), 91 (100), 77 (16), 65 (34), 59 (11), and 41 (15) (Found: C, 65.87; H, 6.21; N, 2.71; S, 5.83. Calcd. for $C_{29}H_{31}NO_6S$: C, 66.78; H, 5.99; N, 2.69; S, 6.15).

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