Nucleophilic Displacement Reactions of 4-(Nosyloxy)-2,3-unsaturated Esters and 2-(Nosyloxy)-3,4-unsaturated Esters

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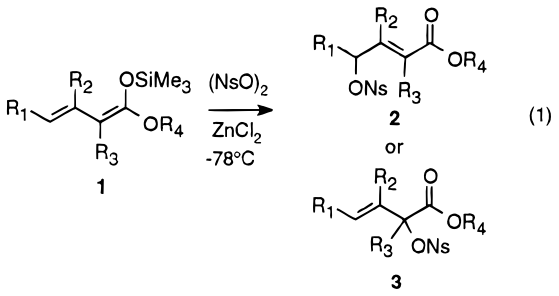
Received March 11, 1996[⊗]

It has been found that 4-(nosyloxy)-2,3-unsaturated esters **2** undergo direct displacement with a wide variety of nucleophiles and yield 4-substituted-2,3-unsaturated products cleanly and in generally good yields. These materials thus have very good synthetic potential for the formation of densely functionalized unsaturated esters. 2-(Nosyloxy)-3,4-unsaturated esters as exemplified by methyl 2-(nosyloxy)-3-butenoate (**3d**) also undergo direct displacement with a range of good nucleophiles; however, the resulting substitution products are prone to rearrangements and tautomerism, as is the starting material itself, so that the synthetic utility of these compounds is limited.

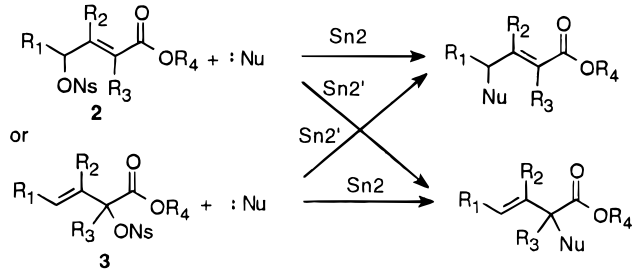
Introduction

In an earlier report we showed that reaction of 1-[(trimethylsilyl)oxy]-1-alkoxy 1,3-dienes **1** with p-nitrobenzenesulfonyl peroxide [$(NsO)_2$] produces 4-(nosyloxy)-2,3-unsaturated esters **2** and 2-(nosyloxy)-3,4-unsaturated esters **3**.[1] By appropriate control, it is possible to achieve good regioselectivity in the formation of **2** and **3** so that each can be prepared in good yield as the major isomer.



Nosylates **2** and **3** are interesting substrates for displacement reactions since they could potentially undergo either direct (S_N2) or indirect (S_N2') substitution to provide either α-substituted *β*,*γ*-unsaturated esters or *γ*-substituted α,*β*-unsaturated esters (Scheme 1). For example, use of an ammonia equivalent nucleophile could produce either a vinylogous amino acid or a vinylglycine analog. Vinylogous amino acids have been of recent synthetic interest because of their occurrence in several drugs,[2] protease inhibitors,[3] and synthetic vinylogous polypeptides of unusual structure.[4] Vinyl amino acids have long been of interest as mechanism-based inhibitors

Scheme 1



of amino acid decarboxylase enzymes.[5] In addition, vinyl amino esters are useful synthetic intermediates in the preparation of kainoid-type natural products[6] and statine derivatives.[7] Other nucleophiles could be expected to yield many other useful products as well.

In looking for literature examples of displacement reactions in similar systems, it rapidly became clear that few have been reported. It has been shown that a 4-bromocrotonate analog of **2** undergoes substitution by benzylamine.[6a] Yamamoto's group has prepared a variety of 4-mesyloxy and 4-tosyloxy analogs of **2** in chiral form and showed that the sulfonate group could be replaced stereospecifically by azide.[8] Most work on these substrates, however, is concerned with the S_N2' displacement of sulfonate by organocuprates to achieve 1,3-chirality transfer.[9] Both 2-chloro[10] and 2-bromo-3,4-unsaturated esters,[5b] which are halogen analogs of **3**, have been prepared. The chloro analog was used as an S_N2' substrate for organocuprates[10] while the 2-bromo compound undergoes direct S_N2 displacement by benzylamine to give a vinyl amino acid product.[5b] Another 2-bromo analog of **3** was shown to undergo direct substitution by ammonia in low yield.[11]

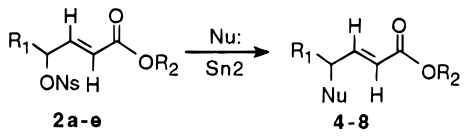
We demonstrated in preliminary studies that several examples of both **2** and **3** undergo direct substitution by

[⊗] Abstract published in *Advance ACS Abstracts,* July 15, 1996.

(1) Hoffman, R. V.; Kim, H.-O. *J. Org. Chem.* **1991**, *56*, 1014.
(2) (a) Cyclotheonamide B: Fusetani, N.; Matsunaga, S.; Matsumoto, Y.; Takebayashi, Y. *J. Am. Chem. Soc.* **1990**, *112*, 7053. Hagihara, M.; Schreiber, S. L. *J. Am. Chem. Soc.* **1992**, *114*, 6570. Wipf, P.; Kim, H.-Y. *Tetrahedron Lett.* **1992**, *33*, 4275. (b) *Keramamide F*: Itagaki, F.; Shigemori, H.; Ishibashi, M.; Nakamura, T.; Sasaki, T.; Kobayashi, J. *J. Org. Chem.* **1992**, *57*, 5540.
(3) (a) Liu, S.; Hanzlik, R. P. *J. Med. Chem.* **1992**, *35*, 1067. (b) Thompson, S. A.; Andrews, P. R.; Hanzlik, R. P. *J. Med. Chem.* **1986**, *29*, 104.
(4) Hagihara, M.; Anthony, N. J.; Stout, T. J.; Clardy, J.; Schreiber, S. L. *J. Am. Chem. Soc.* **1992**, *114*, 6568.
(5) (a) Pederson, M. L.; Berkowitz, D. B. *J. Org. Chem.* **1993**, *58*, 6966 and references therein to the earlier literature. (b) Cardillo, G.; De Simone, A.; Mingardi, A.; Tomasini, C. *Synlett* **1995**, 1131.
(6) (a) Barco, A.; Benetti, S.; Spalluto, G.; Casolari, A.; Pollini, G. P.; Zanirato, V. *J. Org. Chem.* **1992**, *57*, 6279. (b) Roth, P.; Metternich, R. *Tetrahedron Lett.* **1992**, *33*, 3993.
(7) Kogen, H. Nishi, T. *Chem. Commun.* **1987**, 311.
(8) Yamamoto, Y.; Asao, N. *J. Org. Chem.* **1990**, *55*, 5303.
(9) (a) Ibuka, T.; Yamamoto, Y. *Synlett* **1992**, 769. (b) Yamamoto, Y.; Chounan, Y.; Tanaka, M.; Ibuka, T. *J. Org. Chem.* **1992**, *57*, 1024.
(10) Mathew, J. *J. Org. Chem.* **1992**, *57*, 2753.

S0022-3263(96)00477-X CCC: $12.00

Table 1. Reaction of 2a−e with Nucleophiles



2a-e **4-8**

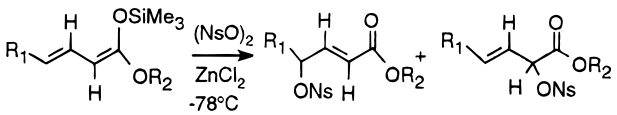
	nucleophile[a]				
reactant	$BnNH_2$ (% **4**)	N_3^- (% **5**)	AcO^- (% **6**)	SCN^- (% **7**)	$S{=}C(NH_2)_2$ (% **8**)
2a		72	93	59	100[b]
2b	87[c]	59	62	94	85
2c	75[c]	41	48	92	60
2d	52	60	58	77	85
2e	60	89			

[a] Isolated yields of purified products [b] Isolated yield of crude product that was >95% pure. [c] Reported previously in ref 1.

benzylamine to produce 4-(benzylamino)-2,3-unsaturated esters and 2-(benzylamino)-3,4-unsaturated esters, respectively.[1] The yields of these displacements were good, and no evidence of indirect (S_N2') substitution was found. On the basis of these results, the present study was initiated to determine the range of nucleophiles which can be incorporated into unsaturated esters by displacement reactions on **2** and **3** and to confirm the generality of the direct nucleophilic displacement pathway (S_N2) that was seen for benzylamine. We present results which show that **2** and **3** react with a variety of nucleophiles by direct displacement. The chemistry of these two systems is sufficiently distinct, however, that they will be discussed separately.

Results

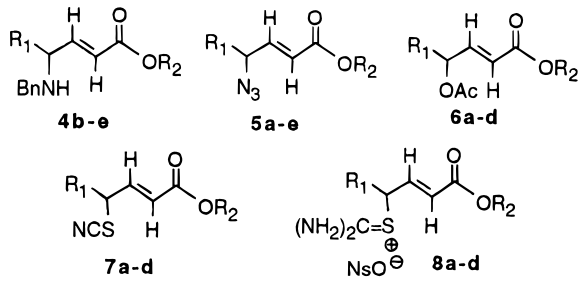
A series of silyloxy dienes **1a−e** was prepared from the corresponding unsaturated esters[1] and reacted with *p*-nitrobenzenesulfonyl peroxide/$ZnCl_2$ in ethyl acetate to give unsaturated nosyloxy esters (eq 2). Dienes **1a−c** which have an alkyl group at C-4 gave only the 4-nosyloxy product **2**. Dienes **1d**,**e** which have only hydrogen substituents at C-2 and C-4 gave 2-nosyloxy ester **3** as the major regioisomer (3:1) The regioisomeric pairs **2d**, **3d** and **2e**, **3e** can be separated effectively by radial chromatography to provide pure samples of **3d**,**e**.[12] Thermolysis of the 3:1 mixture of **3e** and **2e** in refluxing toluene for 24 h produced the thermodynamically more stable **2e** as the only product (80%).[1]



2a-e **3a-e**

1a, R_1=Bn, R_2=Et	100:0	(2)
1b, R_1=Et, R_2=Me	100:0	
1c, R_1=Me, R_2=Me	100:0	
1d, R_1=H, R_2=Me	1 : 3	
1e, R_1=H, R_2=Et	1 : 3	

Reaction of 4-(Nosyloxy)-2,3-unsaturated Esters 2a−e with Nucleophiles. With a source of 4-nosyloxy esters **2a−e** developed, their reactions with nucleophiles were examined. 4-Nosyloxy esters **2a−e** undergo smooth displacement by a range of anionic and neutral nucleophiles. In most cases the 4-substituted products **4−8** were stable and were isolated and purified without difficulty (Table 1).

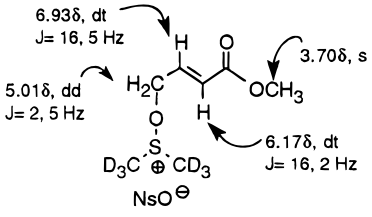


4b-e **5a-e** **6a-d** **7a-d** **8a-d**

In an extension of earlier work,[1] nosylates **2b−e** were reacted with benzylamine and 4-benzylamino esters **4b−e** were obtained in good yields (Table 1). The crude products were of high purity, but **4b**,**c** could be purified further by flash chromatography. In contrast, **4d**,**e** decomposed significantly upon exposure to silica gel, although it was possible to obtain samples of analytically pure **4d**,**e** by flash chromatography.

Reaction of **2a−e** with sodium azide in DMF at 0 °C produced 4-azido esters **5a−e** in good yields (Table 1). Both DMSO and acetonitrile can be used as the solvent equally well. The crude products were relatively pure and could be further purified by bulb to bulb distillation or radial chromatography. The structures of **5a−e** were indicated by an azide band at 2100 cm^{-1}, an ester stretch at 1725 cm^{-1} indicating α,β-unsaturation, and a *trans* coupling constant of 15.6 Hz for the olefinic protons.

Displacement of nosylate by acetate producing acetates **6a−d** was observed upon treatment of **2a−d** with potassium acetate in DMF at room temperature. No reaction was observed when acetonitrile was used as the reaction solvent while the use of DMSO greatly accelerated the reaction (20−60 min versus 3−4 h in DMF). Presumably the rate enhancement results from several factors, the most obvious being the fact that potassium acetate was completely dissolved in DMSO but only partially soluble in DMF. Another cause for the increased rate in DMSO is nucleophilic catalysis in which DMSO displaces the 4-nosyloxy group and is subsequently replaced by acetate. This scenario is supported by the observation that in DMSO-d_6 solution the NMR signals for **1d** are replaced after several hours by a new set of resonances that are assigned to sulfonium salt **9** which results from nosylate displacement in **1d** by DMSO.



9

Reaction of **2a−d** with potassium thiocyanate in acetone gave thiocyanates **7a−d** in high yields (60−94%). The crude 4-thiocyanato-2,3-unsaturated esters were generally obtained in nearly quantitative yields and were >90% pure. They were further purified by bulb to bulb distillation or preparative TLC (**7a**). The thiocyanate

(11) McDonald, I. A.; Palfreyman, M. G.; Jung, M.; Bey, P. *Tetrahedron Lett.* **1985**, *26*, 4091.

(12) It was found that purification by radial chromatography gave consistently higher yields of **2** and **3** than other forms of liquid chromatography. This is presumably due to the shorter contact time with the silica gel surface and implies that the unsaturated nosyloxy esters **2** and **3** begin to decompose on exposure to silica gel.

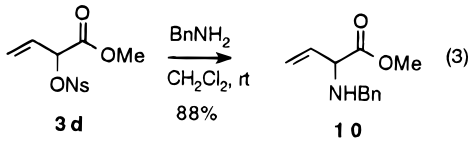
group of **7a**−**d** gave a characteristic strong, sharp IR band at 2150 cm^{-1}.

When reacted with thiourea in acetone, nosylate esters **2a**−**d** afforded 4-isothiouronium-2,3-unsaturated ester salts **8a**−**d** in high yields (60−80%). Although the products are salts, the reaction mixtures remained homogeneous. After removal of the solvent and trituration with dichloromethane, the residue gave **8a**−**d** as solids which were recrystallized from acetone.

These results demonstrate that 4-(nosyloxy)-2,3-unsaturated esters undergo smooth reaction with nucleophiles to give a wide range of 4-substituted-2,3-unsaturated esters in generally good yields. In addition to giving vinylogous amino acid analogs by the incorporation of amines or azide at C-4, oxygen and sulfur nucleophiles can also displace the nosylate group effectively. The results with thiourea can potentially be extended to a vinylog of the sulfide contraction methodology for the synthesis of pyrrolidines.[13]

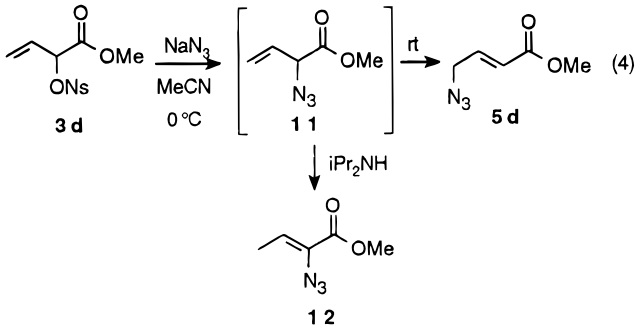
Reaction of 2-(Nosyloxy)-3,4-unsaturated Ester 3d with Nucleophiles. 2-(Nosyloxy)-3,4-unsaturated esters **3** are isolated from reactions of $(NsO)_2$ with silyloxy dienes **1** which lack substituents at either C-2 or C-4 and must be chromatographically separated from their thermodynamically more stable 4-nosyloxy regioisomers **2**. Although they are more difficult to obtain in pure form, they offer the possibility of access to 2-substituted-3,4-unsaturated esters by direct displacement. Therefore **3d** was used as a model to explore the displacement chemistry with a suite of nucleophiles.

Reaction of **3d** with benzylamine in dichloromethane for 4 h led to the formation of benzylamino ester **10** in high yield by direct displacement of nosylate (eq 3). No evidence of **4d** was seen in the NMR spectrum of the crude product. The production of **10** from **3d** is similar to displacement of bromide in a 2-bromo-3,4-unsaturated ester by benzylamine.[5b] The crude product was >90% pure, but attempts to further purify **10** were unsuccessful, as decomposition of the material was observed during chromatography and acid/base extraction.



(3)

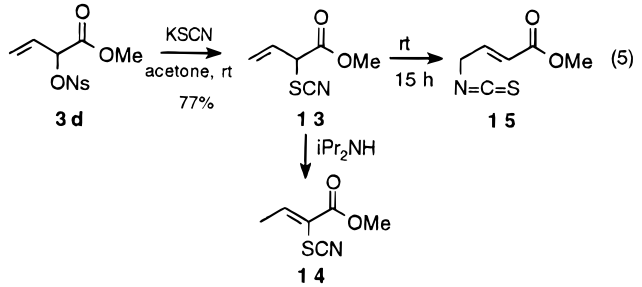
Reaction of **3d** with sodium azide in acetonitrile at room temperature gave methyl 4-azido-2-butenoate (**5d**) as the only product in nearly quantitative yield. The crude product was >90% pure. There was no indication of the formation of the expected 2-azido product. Azide **5d** was obtained in 71% after radial chromatography. While at first sight this result appears to be a case of S_N2' displacement, monitoring of the reaction in acetonitrile-d_3 at 0 °C showed a new set of peaks corresponding to methyl 2-azido-3-butenoate (**11**) as the first-formed product (eq 4). Besides a methoxy singlet (δ 3.75), the α-proton was a one proton doublet at δ 4.59 (J = 6.6 Hz) and there were vinyl signals at δ 5.44δ (2H) and δ 5.95 (1H) for the terminal vinyl group. Upon warming to room temperature, **11** was slowly converted to **5d**. Attempts to isolate **11**, however, gave only **5d**. These results suggest that direct substitution to **11** is followed by a 3,3-sigmatropic rearrangement to produce the ultimate product **5d**. 3,3-Sigmatropic rearrangements in allylic azides are well-known, including a similar rearrangement in a 2-azido-3,4-unsaturated ester which was recently described.[14]



(4)

Confirmation of this scenario was found by carrying out the substitution reaction at 0 °C and then treating the reaction mixture with diisopropylamine. This catalyzed double-bond isomerization in **11** and gave vinyl azide **12**, demonstrating that direct S_N2 displacement is the initial displacement process (eq 4).

The reaction of **3d** with potassium thiocyanate in acetone (15 min) followed by a rapid workup produced 2-thiocyanato ester **13** in 77% yield. A sharp IR band at 2158 cm^{-1} confirmed the presence of the thiocyanate group, and addition of diisopropylamine to the reaction mixture prior to workup gave the vinyl thiocyanate **14**, confirming the direct substitution pathway (eq 5). If the crude product from the reaction was allowed to stand at room temperature overnight, complete conversion to isothiocyanate **15** was seen. Isomerization to the 4-substituted isomer is clearly indicated by the emergence of two vinyl proton signals at δ 6.18 and 6.89 which had a trans coupling constant of J = 15.5 Hz. The isothiocyanate functionality is indicated by a broad,strong IR absorption at 2066−2200 cm^{-1}. In addition the C-4 methylene protons of **15** are shifted downfield to δ 4.38 consistent with an nitrogen atom being bonded to the C-4 carbon atom. Moreover, these spectral data are distinct from **7d**, the 4-thiocyanate analog which has a sharp IR band at 2158 cm^{-1} and methylene protons at δ 3.67. As in the case of azide **11**, formation of **15** presumably occurs by 3,3-sigmatropic rearrangement of initially formed **13**.



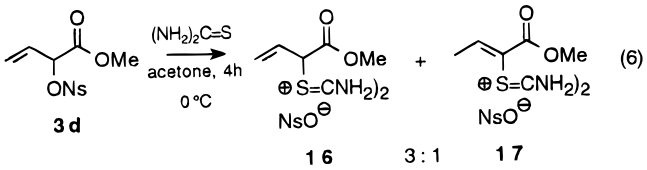
(5)

Reaction of **3d** with thiourea in acetone at 0 °C led to the consumption of the starting material in 4 h. Removal of the solvent gave a mixture of isothiouronium displacement product **16** and vinyl isothiouronium salt **17** (eq 6).

(13) Hernandez, A. S.; Thaler, A.; Castells, J.; Rapoport, H. *J. Org. Chem.* **1996**, *61*, 314 and references therein.

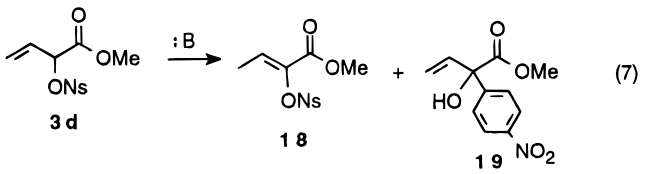
(14) (a) Panek, J. S.; Yang, M.; Muler, I. *J. Org. Chem.* **1992**, *57*, 4063 and references therein to allylic azide rearrangements. (b) See also: Murahashi, S.-I.; Taniguchi, Y.; Imada, Y.; Tanigawa, Y. *J. Org. Chem.* **1989**, *54*, 3292. (c) Naidorf-Meier, S.; Hassner, A. *J. Org. Chem.* **1992**, *57*, 5102.

Storage of the products in the freezer for 1 month resulted in complete conversion to **17**. Alternatively stirring the reaction mixture at room temperature for 5 d gave a quantitative yield of **17**. Salts **16** and **17** were easily distinguished by the vinyl signals in the NMR. Tautomerized salt **17** had a one-proton vinyl quartet at δ 7.91 whereas **16** had three vinyl protons as part of an ABMX system which came at δ 5.49 (2 H) and 5.91 (1 H). From the ^{1}H NMR spectrum of pure **17**, it was possible to extract the NMR spectrum of **16** from the mixture of **16** and **17**. It was not possible to obtain a pure sample of **16** uncontaminated with **17**. The isothiouronium group apparently acidifies the α-proton so that tautomerism takes place under even very mild conditions.



(6)

The use of nucleophiles that were either more basic or less nucleophilic than those described above were generally ineffective in displacement reactions of **3d**. Instead, two base-promoted processes of **3d** were observed. The first is tautomerism of **3d** to vinyl nosylate **18**, and the second is *ipso*-substitution to give p-nitrophenyl alcohol **19** (eq 7).[15] More hindered amines such as piperidine and diisopropylamine or charged bases such as methoxide, acetate, or sulfite in alcohol solvents gave predominately tautomerized **18**. Conversely, anionic bases such as methoxide, acetate, cyanide, and fluoride in aprotic solvents such as DMF or acetonitrile gave mostly *ipso*-product **19**.

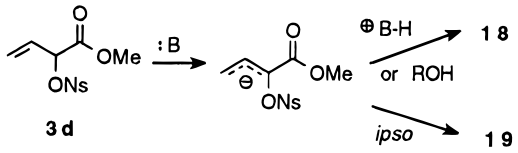


(7)

These results suggest that while good nucleophiles displace the nosylate group in **3d**, the nosylate group also acidifies the α-proton of **3d** significantly and proton removal by the nucleophile/base can compete with displacement if the basicity is high and/or the nucleophilicity is reduced. Under protic conditions the resulting enolate is rapidly reprotonated to give the conjugated vinyl nosylate **18**. In aprotic conditions, either trapping is slower or the enolate is more reactive, and *ipso*-substitution is the primary process of the enolate (Scheme 2). Both processes are detrimental to displacement reactions.

In summary, these results demonstrate that 4-(nosyloxy)-2,3-unsaturated esters **2** undergo direct displacement with a wide variety of nucleophiles and yield 4-substituted-2,3-unsaturated products cleanly and in generally good yields. In addition to the peroxide route to these materials utilized here, these materials can be made by more conventional routes[8,9] and thus have very good synthetic potential for the formation of densely functionalized unsaturated esters. 2-(Nosyloxy)-3,4-unsaturated esters as exemplified by **3d** also undergo

Scheme 2



direct displacement with a range of good nucleophiles; however, the resulting substitution products are prone to rearrangements and tautomerism, as is **3d** itself, so that the synthetic utility of these compounds is limited.

Experimental Section

Melting points are uncorrected. Infrared spectra of liquids were acquired using neat samples, and KBr pellets were used for solids. NMR spectra were acquired in chloroform-*d* solution (unless otherwise noted) at either 400 or 200 MHz, and shifts are reported in ppm relative to tetramethylsilane (TMS). Carbon-13 NMR spectra were obtained at 100 MHz. Thin layer chromatography (TLC) was carried out on 2 × 5 cm glass-supported silica gel 60 F_{254} plates from EM Reagents. Visualization of TLC spots was accomplished with UV irradiation for nosylate compounds, but most other compounds required iodine exposure or oxidation by a spray of aqueous potassium permanganate. Preparative TLC was performed on glass-supported 20 × 20 cm × 250 mm silica gel 60 F_{254} plates. Radial chromatography was performed on 2 mm layers of silica gel 60 F_{254}. Flash chromatography was carried out using a 20 mm × 25 cm column of silica gel 60 (230−400 mesh). Combustion analyses were performed by M-W-H Laboratories, Phoenix, AZ.

Most reagents including methyl and ethyl crotonate, *trans*-2-hexenoic acid, *trans*-2-pentenoic acid, hydrocinnamaldehyde, and triethyl phosponoacetate were purchased from Aldrich. Technical grade *p*-nitrobenzenesulfonyl chloride was purchased from Fluka Chemical Co. and was recrystallized from chloroform and hexane. Most solvents used were HPLC grade. Tetrahydrofuran (THF) was distilled under nitrogen from sodium benzophenone ketyl. The literature method was used for the preparation of *p*-nitrobenzenesulfonyl peroxide.[16] Silyloxy dienes **1b**−**e** and the unsaturated nosyloxy esters **2b**−**e** and **3d**,**e** were prepared by literature methods.[1,17]

Ethyl 5-phenyl-2-pentenoate, the starting material for silyloxy diene **1a** is a known compound; however no data were reported for it. It was prepared in 60% yield using the literature method of carboxyvinylation developed by Wadsworth and Emmons.[18] ^{1}H NMR: δ 1.28 (t, J = 7 Hz, 3H), 2.53 (ddt, J = 1, 7, 8.3 Hz, 2H), 2.78 (dt, J = 7, 8.3 Hz, 2H), 4.18 (q, J = 7 Hz, 2H), 5.85 (dt, J = 1, 15.7 Hz, 1H), 7.01 (dt, J = 7, 15.7 Hz, 1H), 7.30 (m, 5H). ^{13}C NMR: 14.2, 33.9, 34.4, 60.2, 121.9, 126.2, 128.3, 128.5, 140.8, 148.0, 166.5. IR (neat): 3062, 1720, 1656, 1604.0 cm^{-1}. Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.60; H, 7.69. This material was converted to **1a** in the usual way.[1]

Ethyl 5-phenyl-4-[[(*p*-nitrophenyl)sulfonyl]oxy]-2-pentenoate, 2a, was prepared from **1a**. Three identical reactions were carried out, and the products were combined during the workup to give the final crude product. In an oven-dried flask pNBSP (1.21 g, 3 mmol) was dissolved in a room temperature mixture of ethyl acetate (90 mL) and $ZnCl_2$ (800 mg, 6 mmol) and stirred for 30 min until the solution became homogeneous. A dropping funnel was attached, and the apparatus was purged with nitrogen. Silyloxy diene **2a** (1.11 g, 4 mmol) in ethyl acetate (20 mL) was placed into the dropping funnel and added dropwise to the reaction mixture which was cooled to −78 °C. The reaction was stirred for 3 h. Three such reaction solutions were combined, washed with brine (3 × 100 mL), dried ($MgSO_4$), passed through a short pad of silica gel, and

(15) Analogous *ipso*-substitution has been observed previously in α-nosyloxy ketones and esters. Hoffman, R. V.; Jankowski, B. C.; Carr, C. S.; Duesler, E. N. *J. Org. Chem.* **1986**, *51*, 130.

(16) Dannley, R. L.; Gagen, J. E.; Stewart, O. J. *J. Org. Chem.* **1970**, *35*, 3076.

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(18) Wadsworth, W. S., Jr.; Emmons, W. D. *J. Am. Chem. Soc.* **1961**, *83*, 1733.

concentrated under reduced pressure to give a brown oil (3.86 g). Flash chromatography (hexane−ethyl acetate, 95:5 to 9:1) gave **2a** as a white solid (1.25 g, 34%): mp 92−4 °C; ^{1}H NMR 1.29 (t, J = 7 Hz, 3H), 2.98 (ABm, 2H), 4.20 (q, J = 7 Hz, 2H), 5.29 (dd, J = 1.3, 5.8 Hz, 1H), 6.07 (dd, J = 1.3, 15.8 Hz, 1H), 6.87 (dd, J = 5.8, 15.8 Hz, 1H), 7.10 (m, 5H), 7.74 and 8.16 (ABq, J = 8.6 Hz, 4H); ^{13}C NMR 14.6, 41.0, 61.0, 82.9, 124.1, 124.2, 127.3, 128.7, 128.8, 129.4, 134.7, 141.9, 142.0, 150.4, 165.2; IR (KBr) 1716, 1664, 1608 cm^{-1}. Anal. Calcd for $C_{19}H_{19}NSO_7$: C, 56.29; H, 4.72; N, 3.46. Found: C, 56.15; H, 4.78; N, 3.48.

Methyl 4-(*N*-benzylamino)-2-butenoate, 4d, was prepared by the following general method. Nosylate **2d** (280 mg, 0.93) and benzylamine (360 mg, 3.4 mmol) in dichloromethane (20 mL) were stirred at room temperature for 24 h. The cloudy white solution was concentrated, and ethyl acetate (100 mL) was added. The solution was washed with brine (2 × 100 mL) and dried ($MgSO_4$), and the cloudy white solution was passed through a short pad of silica gel to give crude **4d** as a yellow oil (100 mg) which was greater than 95% pure by ^{1}H NMR analysis. Separation by preparative TLC (hexane−ethyl acetate, 100:0 to 90:10) gave analytically pure **9d** as a yellow oil (50 mg, 26%): ^{1}H NMR 1.75 (s, 1H, 3.43 (dd, J = 1.8, 5.4 Hz, 2H), 3.74 (s, 3H), 3.81 (s, 2H), 6.04 (dt, J = 1, 8, 15.8 Hz, 1H), 7.03 (dt, J = 5.4, 15.8 Hz, 1H), 7.32 (m, 5H); ^{13}C NMR 49.5, 51.5, 53.3, 121.2, 127.2, 128.1, 128.5, 139.7, 146.9, 166.9; IR (neat) 1726, 1661, 1606 cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.40; H, 7.21; N, 6.97.

Ethyl 4-(*N*-benzylamino)-2-butenoate, 4e, was prepared from **2e** (240 mg, 0.77 mmol) and benzylamine (290 mg, 2.7 mmol) by the same procedure. The crude product was a yellow oil (180 mg) which showed four spots by TLC. Ethyl acetate (30 mL) was added, and the solution was extracted with 1 N HCl (30 mL and then 20 mL) and water (100 mL) to obtain a colorless aqueous phase (the organic phase was yellow). The aqueous phase was washed with ethyl acetate (2 × 100 mL) and then made basic by the addition of 10% NaOH (40 mL). The basic aqueous solution was extracted with ethyl acetate (2 × 100 mL), and the resulting organic phase was washed with brine (2 × 100 mL), dried ($MgSO_4$), and concentrated to give **4e** as a colorless oil (100 mg, 60%) which was greater than 95% pure by ^{1}H NMR. An analytical sample was obtained by preparative TLC (hexane−ethyl acetate, 95:5) as a colorless oil: ^{1}H NMR 1.29 (t, J = 7.1 Hz, 3H), 1.54 (broad s, 1H), 3.43 (dd, J = 1.8, 3.7 Hz, 2H), 3.81 (s, 2H), 4.20 (q, J = 7.1 Hz, 2H), 6.03 (dt, J = 1.8, 15.8 Hz, 1H), 7.02 (dt, J = 3.7, 15.8 Hz, 1H), 7.33 (m, 5H); ^{13}C NMR 14.3, 49.5, 53.3, 60.3, 121.7, 127.1, 128.1, 128.5, 139.8, 146.6, 166.4; IR (neat) 1718, 1658 cm^{-1}. Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81. Found: C, 71.20; H, 7.55.

Methyl 4-(*N*-benzylamino)-2-pentenoate, 4c, was prepared from **2c** (150 mg, 0.45 mmol) and benzylamine (190 mg, 1.7 mmol) in dichloromethane (20 mL) with stirring at room temperature for 6 days. Amine **9c** was isolated as a yellow oil (70 mg) which was about 90% pure by ^{1}H NMR. The observed spectrum matched the spectrum of an authentic sample.[1]

Ethyl 4-azido-5-phenyl-2-pentenoate, 5a, was prepared by the following general method. Nosylate **2a** (170 mg, 0.42 mmol) and sodium azide (60 mg, 0.9 mmol) were stirred in acetonitrile (10 mL) at room temperature for 4 h. The reaction was quenched with a solution of saturated ammonium chloride (6 mL) and aqueous ammonium hydroxide (2 mL). The solution was extracted with ethyl acetate (100 mL). The organic phase was washed with brine (2 × 100 mL), dried ($MgSO_4$), passed through a short pad of silica gel, and concentrated under reduced pressure to give **5a** as a yellow oil (74 mg) which was greater than 95% pure by ^{1}H NMR. Purification by flash chromatography (hexane−ethyl acetate, 100:0 to 95:5 to 90:10) gave **5a** as a colorless oil (50 mg, 33%): ^{1}H NMR 1.29 (t, J = 7.2 Hz, 3H), 2.89 (d, J = 7 Hz, 2H), 4.21 (q + m, J = 7.2 Hz, 3H), 6.01 (d, J = 16 Hz, 1H), 6.85 (dd, J = 7, 16 Hz, 1H), 7.30 (m, 5H); ^{13}C NMR 14.2, 40.6, 60.7, 63.82 123.4, 127.1, 128.7, 129.4, 136.2, 143.7, 165.6; IR (neat) 1720, 1658, 1604 cm^{-1}. Anal. Calcd for $C_{13}H_{15}N_3O_2$: C, 63.66; H, 6.16; N, 17.13. Found: C, 63.70; H, 6.03; N, 17.06.

Methyl 4-azido-2-hexenoate, 5b, was prepared from **2b** (200 mg, 0.61 mmol) and sodium azide (80 mg, 1.2 mmol) using a 4 h reaction time at 0 °C (yellow oil, 100 mg). Purification by Kugelrohr distillation with a bath temperature of 35−40 °C/0.5 mmHg gave **5b** as a colorless oil (60 mg, 59%): ^{1}H NMR 0.99 (t, J = 7 Hz, 3H), 1.67 (pent, J = 7 Hz, 2H), 3.77 (s, 3H), 3.96 (dt, J = 6.4, 7 Hz, 1H), 6.04 (d, J = 15.6 Hz, 1H), 6.80 (dd, J = 6.4, 15.6 Hz, 1H); ^{13}C NMR 10.1, 27.2, 51.8, 64.0, 122.8, 144.65, 166.2; IR (neat) 1731, 1666 cm^{-1}. Anal. Calcd for $C_7H_{11}N_3O_2$: C, 49.7; H, 6.55; N, 24.84. Found: C, 49.58; H, 6.67; N, 24.68.

Methyl 4-azido-2-pentenoate, 5c, was prepared from **2c** (200 mg, 0.63 mmol) and sodium azide (80 mg, 1.2 mmol) using a 3.5 h reaction time at 0 °C (yellow oil, 50 mg). Purification by Kugelrohr distillation with a bath temperature of 35−40 °C/0.5 mmHg gave **5c** as a colorless oil (40 mg, 41%): ^{1}H NMR 1.38 (d, J = 7 Hz, 3H), 3.77 (s, 3H), 4.17 (m, 1H), 6.03 (dd, J = 1, 15.6 Hz, 1H), 6.84 (dd, J = 6, 15.6 Hz, 1H); ^{13}C NMR 19.2, 51.8, 57.5, 121.9, 145.8, 166.3; IR (neat) 1730, 1662 cm^{-1}. Anal. Calcd for $C_6H_9N_3O_2$: C, 46.45; H, 5.85. Found: C, 46.26; H, 6.00.

Methyl 4-azido-2-butenoate, 5d, was prepared from **2d** (300 mg, 1.0) and sodium azide (130 mg, 2.0 mmol) in DMF (10 mL) at 0 °C for 3 h as a colorless oil (110 mg, 60%) after separation by radial chromatography (hexane−ethyl acetate, 95:5 to 90:10): ^{1}H NMR 3.77 (s, 3H), 4.01 (dd, J = 1.6, 5.3 Hz, 2H), 6.10 (dt, J = 1.6, 15.6 Hz, 1H), 6.91 (dt, J = 5.3, 15.6 Hz, 1H); ^{13}C NMR 51.2, 51.8, 123.3, 140.7, 166.1; IR (neat) 1725, 1666 cm^{-1}. Anal. Calcd for $C_5H_7N_3O_2$: C, 42.55; H, 5.00; N, 29.77. Found: C, 42.67; H, 5.15; N, 29.56.

Ethyl 4-azido-2-butenoate, 5e, was prepared from **2e** (420 mg, 1.4 mmol) and sodium azide (182 mg, 2.8 mmol) in DMF (10 mL) at 0 °C for 3 h as a colorless oil (120 mg, 55%) after purification by radial chromatography (hexane−ethyl acetate, 95:5): ^{1}H NMR 1.31 (t, J = 7.1 Hz, 3H), 4.01 (dd, J = 1.7, 5.2 Hz, 2H), 4.23 (q, J = 7.1 Hz, 2H), 6.09 (dt, J = 1.7, 15.6 Hz, 1H), 6.90 (dt, J = 5.2, 15.6 Hz, 1H); ^{13}C NMR 14.2, 51.2, 60.7, 123.7, 140.35, 165.6; IR (neat) 1722, 1662 cm^{-1}. Anal. Calcd for $C_6H_9N_3O_2$: C, 46.40; H, 5.84; N, 27.05. Found: C, 46.19; H, 5.63; N, 26.94.

Ethyl 4-acetoxy-5-phenyl-2-pentenoate, 6a, was prepared by the following general procedure. Nosylate **2a** (250 mg, 0.62 mmol) and potassium acetate (120 mg, 1.2 mmol) were stirred in DMF (10 mL) at room temperature for 4 h. Ethyl acetate (100 mL) was added, and the solution was washed with brine (2 × 100 mL), dried ($MgSO_4$), passed through a short pad of silica gel, and concentrated under reduced pressure to give crude **6a** as a yellow oil (150 mg) which was approximately 95% pure by ^{1}H NMR. Purification of 70 mg of the crude product by preparative TLC gave **6a** as a colorless oil (30 mg, 39%): ^{1}H NMR 1.27 (t, J = 7.1 Hz, 3H), 2.03 (s, 3H), 2.96 (AB of ABX, J = 6, 7 Hz, 2H), 4.18 (q, J = 7.1 Hz, 2H), 5.60 (m, 1H), 5.91 (dd, J = 1.5, 15.6 Hz, 1H), 6.88 (dd, J = 5.5, 15.6 Hz, 1H), 7.25 (m, 5H); ^{13}C NMR 14.2, 20.9, 40.4, 60.6, 73.0, 122.0, 126.9, 128.5, 129.4, 136.0, 144.4, 165.9, 169.8; IR (neat) 1743, 1720, 1662, 1627, 1601 cm^{-1}. Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.69; H, 6.92. Found: C, 68.87; H, 6.87.

Methyl 4-acetoxy-2-hexenoate, 6b, was prepared from **2b** (200 mg, 0.61 mmol) and potassium acetate (120 mg, 1.2 mmol) in DMSO (10 mL) at room temperature for 1 h as a colorless oil (110 mg). Purification by Kugelrohr distillation with a bath temperature of 35−40 °C/0.5 mmHg gave **6b** as a colorless oil (70 mg, 62%): ^{1}H NMR 0.93 (t, J = 7.6 Hz, 3H), 1.71 (m, 2H), 2.10 (s, 3H), 3.75 (s, 3H), 5.35 (m, 1H), 5.95 (dd, J = 1.6, 15.6 Hz, 1H), 6.85 (dd, J = 5.6, 15.6 Hz, 1H); ^{13}C NMR 9.2, 21.0, 26.9, 51.7, 73.5, 121.3, 145.5, 166.4, 170.1; IR (neat) 1746, 1726, 1664 cm^{-1}. Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 58.02; H, 7.62.

Methyl 4-acetoxy-2-pentenoate, 6c, was prepared from **2c** (150 mg, 0.48 mmol) and potassium acetate (94 mg, 0.96 mmol) in DMSO (10 mL) at room temperature for 1 h as a pale yellow oil (60 mg) which was homogeneous by TLC. Purification by Kugelrohr distillation with a bath temperature of 35−40 °C/0.5 mmHg gave **6c** as a colorless oil (40 mg, 48%): ^{1}H NMR 1.37 (d, J = 6.4 Hz, 3H), 2.09 (s, 3H), 3.75 (s,

3H), 5.49 (ddq, J = 1.2, 5, 6.4 Hz, 1H), 5.97 (dd, J = 1.2, 16 Hz, 1H), 6.88 (dd, J = 5, 16 Hz, 1H); ^{13}C NMR 19.6, 21.1, 51.7, 68.8, 120.6, 146.6, 166.5, 169.9; IR (neat) 1751, 1730, 1664 cm^{-1}. Anal. Calcd for $C_8H_{12}O_4$: C, 55.81; H, 7.03. Found: C, 55.61; H, 7.25.

Methyl 4-acetoxy-2-butenoate, 6d, was prepared from **2d** (100 mg, 0.33 mmol) and sodium acetate trihydrate (92 mg, 0.68 mmol) in DMF (10 mL) at room temperature for 1.5 h as a pale yellow oil (30 mg) which was 95% pure by ^{1}H NMR. Purification by preparative TLC gave **6d** as a colorless oil (20 mg, 15%): ^{1}H NMR 2.13 (s, 3H), 3.76 (s, 3H), 4.75 (dd, J = 2, 4.6 Hz, 2H), 6.04 (dt, J = 2, 15.8 Hz, 1H), 6.96 (dt, J = 4.6, 15.8 Hz, 1H); ^{13}C NMR 20.7, 51.8, 62.6, 121.8, 141.5, 166.3, 170.3; IR (neat) 1726, 1666 cm^{-1}. Anal. Calcd for $C_7H_{10}O_4$: C, 53.16; H, 6.37. Found: C, 52.96; H, 6.45.

Ethyl 4-thiocyanato-5-phenyl-2-pentenoate, 7a, was prepared by the following general procedure. Nosylate **2a** (180 mg, 0.44 mmol) and potassium thiocyanate (86 mg, 0.88 mmol) were stirred in acetone (10 mL) at room temperature for 3 h. The solution was concentrated under reduced pressure, ethyl acetate (100 mL) was added, and the cloudy white solution was passed through a short pad of silica gel. Some additional white solid formed after filtration. The solvent was removed by rotary evaporation, chloroform (50 mL) was added, and the solid was removed by filtration. The solution was evaporated under reduced pressure to give a crude product, **7a**, as a yellow oil (120 mg). Purification of 60 mg of the crude product by preparative TLC (hexane−ethyl acetate, 95:5 to 90:10) gave **7a** as colorless oil (34 mg, 59%): ^{1}H NMR 1.22 (t, J = 7.1 Hz, 3H), 3.04 and 3.06 (two ABq's, J = 9.6, 14.2 Hz, 2H), 4.04 (dt, J = 8.6, 9.6 Hz, 1H), 4.11 (7.1, 2H), 5.91 (d, J = 15.6 Hz, 1H), 6.85 (dd, J = 8.6, 15.6 Hz, 1H), 7.28 (m, 5H); ^{13}C NMR 14.2, 39.9, 51.9, 61.0, 110.2, 124.9, 127.7, 128. 9, 129.1, 135.5, 142.46, 165.1; IR (neat) 2154, 1718, 1652, 1606 cm^{-1}. Anal. Calcd for $C_{14}H_{15}NSO_2$: C, 64.34; H, 5.79; N, 5.36. Found: C, 64.38; H, 5.71; N, 5.19.

Methyl 4-thiocyanato-2-hexenoate, 7b, was prepared from **2b** (170 mg, 0.52 mmol) and KSCN (100 mg, 1.0 mmol) in acetone (10 mL) at room temperature for 3 h as a colorless oil (90 mg) which showed a single component by TLC and was approximately 95% pure by ^{1}H NMR. Kugelrohr distillation with a bath temperature of 45−50 °C/0.5 mmHg gave **7b** as a colorless oil (50.6 mg, 53%): ^{1}H NMR 1.08 (t, J = 7.2 Hz, 3H), 1.90 (dq, J = 7.2, 8 Hz, 2H), 3.78 (s, 3H), 6.04 (d, J = 15.6 Hz, 1H), 6.86 (dd, J = 8, 15.6 Hz, 1H); ^{13}C NMR 11.6, 27., 51.8, 52.0, 110.2, 124.2, 143.2, 165.7; IR (neat) 2154, 1728, 1656 cm^{-1}. Anal. Calcd for $C_8H_{11}NSO_2$: C, 51.87; H, 5.99. Found: C, 51.80; H, 5.90.

Methyl 4-thiocyanato-2-pentenoate, 7c, was prepared from **2c** (140 mg, 0.44 mmol) and KSCN (86 mg, 0.88 mmol) in acetone (10 mL) at room temperature for 3 h as a yellow oil (70 mg) which was >90% pure by ^{1}H NMR. Purification by Kugelrohr distillation with a bath temperature of 50−55 °C/0.5 mmHg gave **7c** as a colorless oil (43.4 mg, 57%): ^{1}H NMR 1.63 (d, J = 6.9 Hz, 3H), 3.78 (s, 3H), 4.04 (dq, J = 1.1, 6.9 Hz, 1H), 6.01 (dd, J = 1.1, 15.6 Hz, 1H), 6.93 (dd, J = 6.9, 15.6 Hz, 1H); ^{13}C NMR 19.8, 44.7, 52.0, 110.2, 123.4, 144.2, 165.7; IR (neat) 2154, 1726, 1656 cm^{-1}. Anal. Calcd for $C_7H_9NSO_2$: C, 49.11; H, 5.30; N, 8.18. Found: C, 48.90; H, 5.53; N, 7.98.

Methyl 4-thiocyanato-2-butenoate, 7d, was prepared from **2d** (100 mg, 0.33 mmol) and KSCN (60 mg, 0.62 mmol) in acetonitrile (10 mL) at 0 °C for 2 h as a yellow oil (40 mg) which appeared to be a single component by TLC. Purification by preparative TLC (hexane−ethyl acetate, 100:0 to 90:10) gave **7d** as a colorless oil (20 mg, 38%): ^{1}H NMR 3.67 (dd, J = 1.0, 7.5 Hz, 2H), 3.79 (s, 3H), 6.11 (dt, J = 1.0, 15.4 Hz, 1H), 6.96 (dt, J = 7.5, 15.4 Hz, 1H); ^{13}C NMR 34.4, 52.0, 110.8, 126.1, 138.6, 165.5; IR (neat) 2156, 1724, 1658 cm^{-1}. Anal. Calcd for $C_6H_7NSO_2$: C, 45.85; H, 4.49; N, 8.91; S, 20.40. Found: C, 46.03; H, 4.62; N, 8.72; S, 20.16.

Methyl 4-isothiouronium-2-hexenoate *p*-nitrobenzenesulfonate, 8b, was prepared by the following general procedure. Nosylate **2b** (74.4 mg, 0.226 mmol) and thiourea (27 mg, 0.36 mmol) were dissolved in acetone (10 mL) and stirred at 50 °C for 8 h. The clear reaction solution was concentrated, CH_2Cl_2 (10 mL) was added, and the solution was cooled in a freezer overnight to give **8b** as white crystals (78 mg), mp 119−122 °C, which were essentially pure by ^{1}H NMR. Recrystallization from hot acetone gave pure **8b** (20 mg, 22%): mp 151−152 °C; ^{1}H NMR (DMSO-d_6) 0.94 (t, J = 8 Hz, 3H), 1.77 (dq, J = 7, 8 Hz, 2H), 4.45 (dt, J = 7, 9 Hz, 1H), 6.09 (d, J = 15.6 Hz, 1H), 6.74 (dd, J = 9, 15.6 Hz, 1H), 7.84 and 8.21 (ABq, J = 8 Hz, 4H), 9.06 and 9.17 (two broad s, 4H); ^{13}C NMR (DMSO-d_6) 11.1, 25.4, 47.5, 51.61, 122.6, 123.2, 126.8, 144.8, 147.2, 154.2, 165.3, 167.3; IR (KBr) 1949, 1724, 1678, 1656, 1604 cm^{-1}. Anal. Calcd for $C_{14}H_{19}N_3S_2O_7$: C, 41.47; H, 4.72. Found: C, 41.36; H, 4.86.

Ethyl 4-isothiouronium-5-phenyl-2-pentenoate *p*-nitrobenzenesulfonate, 8a, was prepared from **2a** (100 mg, 0.25 mmol) and thiourea (18.8 mg, 0.247 mmol) in refluxing acetone (20 mL) for 2 days (TLC monitoring) as a yellow oil (120 mg, 100%) which was soluble in acetone: ^{1}H NMR (acetone-d_6) 1.21 (t, J = 7.1 Hz, 3H), 3.17 (dd, J = 7.4, 7.6 Hz, 2H), 4.13 (q, J = 7.1 Hz, 2H), 5.01 (m, 1H), 6.12 (d, J = 15.6 Hz, 1H), 6.88 (dd, J = 6.5, 15.6 Hz, 1H), 7.30 (m, 5H), 7.69 and 8.27 (ABq, J = 8.9 Hz, 4H), 8.72 and 9.56 (two broad s, 4H). This material was not characterized further.

Methyl 4-isothiouronium-2-pentenoate *p*-nitrobenzenesulfonate, 8c, was prepared from **2c** (80.0 mg, 0.25 mmol) and thiourea (19.3 mg, 0.25 mmol) in refluxing acetone (10 mL) for 15 h as a crude white solid (99.3 mg). Recrystallization from hot acetone gave **8c** (60 mg, 60%) as a white solid: mp 161−4 °C; ^{1}H NMR (DMSO-d_6) 1.44 (d, J = 6.9 Hz, 3H), 3.69 (s, 3H), 4.63 (m, 1H), 6.01 (d, J = 15.6 Hz, 1H), 6.82 (dd, J = 8.3, 15.6 Hz, 1H), 7.86 and 8.23 (ABq, J = 8.9 Hz, 4H), 9.11 and 9.21 (two broad s, 4H); ^{13}C NMR (DMSO-d_6) 20.7, 43.4, 54.1, 124.1, 125.7, 129.27, 148.3, 149.7, 156.5, 167.9, 169.7; IR (KBr) 1930, 1728, 1674, 1668.0, 1602 cm^{-1}. Anal. Calcd for $C_{13}H_{17}N_3S_2O_7$: C, 39.89; H, 4.38. Found: C, 40.00; H, 4.24.

Methyl 4-isothiouronium-2-butenoate *p*-nitrobenzenesulfonate, 8d, was prepared from **2d** (50.0 mg, 0.166 mmol) and thiourea (13.0 mg, 0.17 mmol) in acetone (10 mL) at room temperature for 2 h as a white solid (53.5 mg, 85%) after recrystallization from hot acetone: mp 169−171 °C; ^{1}H NMR (DMSO-d_6) 3.69 (s, 3H), 4.04 (dd, J = 1, 7 Hz, 2H), 6.13 (dt, J = 1, 15.6 Hz, 1H), 6.83 (dt, J = 7, 15.6 Hz, 1H), 7.84 and 8.21 (ABq, J = 8.9 Hz, 4H), 9.1 (broad s, 4H); ^{13}C NMR (DMSO-d_6) 30.6, 51.6, 123.3, 123.6, 126.8, 141.2, 147.3, 153.9, 165.3, 168.3; IR (KBr) 1722, 1682, 1670, 1602.0 cm^{-1}. Anal. Calcd for $C_{12}H_{15}N_3S_2O_7$: C, 38.19; H, 4.01; N, 11.13; S, 16.99. Found: C, 38.39; H, 4.25; N, 10.93; S, 16.79.

Methyl 2-(*N*-benzylamino)-3-butenoate, 10, was prepared from **3d** (50 mg, 0.17 mmol) and benzylamine (70 mg, 0.67) in dichloromethane (20 mL) by stirring at room temperature for 24 h. Amine **10** was obtained as a yellow oil (30 mg) which contained several impurities by ^{1}H NMR. The observed spectra of the major component (>90%) was in agreement with the reported spectra of **14**.[1,17] None of the 4-amino isomer **4d** was detected in the products. The sample decomposed during an attempted separation by preparative TLC on silica gel.

Reactions of 3d with Sodium Azide. Reaction of **3d** (300 mg, 1.0 mmol) and sodium azide (130 mg, 2.0 mmol) in acetonitrile (10 mL) at room temperature for 1.5 h gave **5d** as a colorless oil (100 mg, 71%) after purification by radial chromatography. When a mixture of **3d** (50 mg, 0.166 mmol) and sodium azide (11 mg, 0.17 mmol) was stirred in acetonitrile-d_3 (5 g) at 0 °C for 2 h, examination of an aliquot by ^{1}H NMR showed that it was a mixture of methyl 2-azido-3-butenoate, **11**, and **5d** along with a small amount of starting material **3d** (70:25:5). From this sample was obtained the ^{1}H NMR spectrum of **11**: ^{1}H NMR 3.75 (s, 3H), 4.59 (d, J = 6.6 Hz, 1H), 5.44 (dd, J = 6, 13 Hz, 2H), 5.95 (m, 1H). Reaction of **3d** (140.0 mg, 0.465 mmol) and sodium azide (30.2 mg, 0.465 mmol) in acetonitrile (15 mL) at 0 °C for 4 h followed by addition of diisopropylamine (six drops) caused isomerization of **11** to **12.** After workup the crude product was a yellow oil (40 mg) which contained methyl 2-azido-2-butenoate (**12**) as the major component (ca. 25% yield by NMR). The ^{1}H NMR for **12** obtained in this mixture confirms its structure: ^{1}H NMR 1.80 (d, J = 7 Hz, 3H), 3.83 (s, 3H), 6.26 (q, J = 7 Hz, 1H).

Particularly revealing is the vinyl quartet at δ 6.26 coupled to the allylic methyl doublet at δ 1.8.

Reactions of 3d with Potassium Thiocyanate. A mixture of **3d** (50.0 mg, 0.166 mmol) and KSCN (17 mg, 0.17 mmol) in acetone-d_6 (5 mL) was stirred at room temperature for 15 min. The white solid was filtered off, and the resulting solution contained only methyl 2-thiocyanato-3-butenoate (**13**) by ^{1}H NMR. The solution was immediately concentrated under reduced pressure to give the crude product, **13**, as a yellow oil (20 mg). This compound was not stable enough for ^{13}C NMR or combustion analysis, but its ^{1}H NMR and IR spectra confirmed its structure as **13**. ^{1}H NMR 3.84 (s, 3H), 4.85 (d, J = 8.9 Hz, 1H), 5.52 and 5.56 (two d, J = 5.4 and 9.9 Hz, 2H,), 6.01 (m, 1H); IR (neat) 2158.0 (sharp), 1742.0, 1634.0 cm^{-1}.

Reaction of **3d** (63.1 mg, 0.209 mmol) and KSCN (20.4 mg, 0.21 mmol) in acetone (5 mL) at 0 °C for 3 h followed by addition of diisopropylamine (three drops) and stirring at 0 °C for 10 min gave **14** was a yellow oil (29.3 mg). Purification by bulb to bulb distillation with a bath temperature of 50−55 °C/0.5 mmHg gave **14** as a colorless oil (9.7 mg, 30%). Trace impurities were observed by NMR so no combustion analysis was performed. **14**: ^{1}H NMR 2.20 (d, J = 7.1 Hz, 3H), 3.89 (s, 3H), 7.65 (q, J = 7.1 Hz, 1H); ^{13}C NMR 17.4, 53.4, 109.2, 119.5, 152.6, 163.0; IR (neat) 2162, 1727, 1622 cm^{-1}.

Reaction of **3d** (300 mg, 1 mmol) and KSCN (196 mg, 2 mmol) in acetonitrile (10 mL) at 0 °C for 1.5 h gave a yellow oil (110 mg) which was a mixture of **13** and **15** (40:60). After neat overnight stirring, the mixture contained only isothiocyanate **15**. Purification by preparative TLC (hexane−ethyl acetate, 95:5) gave methyl 4-isothiocyano-2-butenoate (**15**) as a colorless oil (20 mg, 13%). ^{1}H NMR 3.78 (s, 3H), 4.38 (dd, J = 2, 4 Hz, 2H), 6.18 (dt, J = 2, 15.5 Hz, 1H), 6.89 (dt, J = 4, 15.5 Hz, 1H); IR (neat) 2060 (br), 1728, 1666 cm^{-1}. Insufficient material was available for purification to analytical purity.

Reactions of 3d with Thiourea. Methyl 2-isothiouronium-3-butenoate *p*-nitrobenzenesulfonate, **16**, was prepared from **3d** (50.0 mg, 0.166 mmol) and by stirring with thiourea (13 mg, 0.17) in acetone (10 mL) at room temperature for 3 h. The solvent was removed by under reduced pressure, dichloromethane (10 mL) was added, and a white solid mp 72−5 °C (47.7 mg), crystallized out of solution upon addition of hexane (ca. 3 mL) and storing in the freezer overnight. The solid product was a mixture of **16** and tautomer **17** (90:10) and was soluble in chloroform. The spectrum of **16** could be obtained from the spectrum of the mixture, and the spectra of an authentic sample of **17**. **16**: ^{1}H NMR 3.79 (s, 3H), 5.07 (d, J = 7.9 Hz, 1H), 5.42 (d, J = 10.3 Hz, 1H), 5.51 (d, J = 17 Hz, 1H), 5.88 (m, 1H), 8.01 and 8.02 (ABq, J = 8.6 Hz, 4H), 8.6 (s, 2H), 9.6 (s, 2H); IR (neat) 1742, 1682, 1601 cm^{-1}.

An authentic sample of methyl 2-isothiouronium-2-butenoate *p*-nitrobenzenesulfonate, **17**, was prepared from **3d** (50.0 mg, 0.166 mmol) and thiourea (13.0 mg, 0.17 mmol) in acetone (10 mL) by stirring at 0 °C for 4 h followed by storing in the freezer for 1 month. No solid formed during the reaction. The solvent was removed, and dichloromethane (10 mL) and hexane (ca. 3 mL) were added to give crystallization of **17** as a white solid (41 mg), mp 74−8 °C. An analytical sample was obtained by recrystallization from acetone/hexane: mp 215−216 °C (white solid); ^{1}H NMR 2.15 (d, J = 7 Hz, 3H), 3.79 (s, 3H), 7.91 (q, J = 7 Hz, 1H), 8.01 and 8.24 (ABq, J = 8 Hz, 4H), 8.6 (s, 2H) 9.2 (s, 2H); ^{13}C NMR (DMSO-d_6) 18.1, 53.5, 119.0, 124.0, 127.4, 147.2, 154.5, 159.7, 163.8, 168.5; IR (KBr) 1702, 1670, 1606 cm^{-1}. Anal. Calcd for $C_{12}H_{15}N_3S_2O_7$: C, 38.19; H, 4.01. Found: C, 38.45; H, 4.35.

Salt **17** could also be prepared from **3d** (50.0 mg, 0.166 mmol) and thiourea (13.0 mg, 0.17 mmol) in acetone (10 mL) by stirring at room temperature for 5 days. No solid formed during the reaction. The solvent was removed to give the crude **17** as a colorless oil (63 mg) which did not contain any **16** by ^{1}H NMR.

Methyl 2-[[(*p*-nitrophenyl)sulfonyl]oxy]-2-butenoate, 18, was produced as a major product in the reaction of **3d** with bases under protic conditions. For example, a mixture of **3d** (50.0 mg, 0.166 mmol) and diisopropylamine (70 mg, 0.69 mmol) in dichloromethane (30 mL) was stirred at room temperature overnight. TLC showed that the reaction was about 40% complete in half an hour. The solvent was removed, ethyl acetate (50 mL) was added, and the solution was washed with 5% HCl (50 mL) and brine (2 x 100 mL), dried (MgSO4), and concentrated under reduced pressure to give the crude product **18** as a yellow oil (50 mg) which was about 95% pure by ^{1}H NMR. Purification by preparative TLC (hexane−ethyl acetate, 80:20) gave **18** as a colorless oil (20, 40%): ^{1}H NMR 1.93 (d, J = 7 Hz, 3H), 3.69 (s, 3H), 6.89 (q, J = 7 Hz, 1H), 8.24 and 8.43 (ABq, J = 9 Hz, 4H); ^{13}C NMR 12.7, 52.6, 124.1, 129.8, 132.9, 137.9, 142.4, 150.9, 161.6; IR (neat) 1735, 1663, 1608 cm^{-1}. Anal. Calcd for $C_{11}H_{11}NSO_7$: C, 43.86; H, 3.68; N, 4.65; S, 10.64. Found: C, 43.61; H, 3.76; N, 4.50; S, 10.81.

Methyl 2-(*p*-nitrophenyl)-2-hydroxy-3-butenoate, 19, was produced as the major product from the reaction of **3d** with anionic bases in aprotic conditions. For example, a mixture of **3d** (270 mg, 0.90 mmol) and sodium cyanide (90 mg, 1.8 mmol) in acetonitrile (9 mL) was stirred at room temperature for 21 h. The solution was concentrated, ethyl acetate (50 mL) was added, and the organic phase was washed with water (3 × 50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The crude product, **19**, was a yellow oil (190 mg, 80%) which was about 95% pure by ^{1}H NMR. An analytical sample of **19** was obtained by preparative TLC (hexane−ethyl acetate, 90:10 to 80:20): ^{1}H NMR 3.85 (s, 3H), 4.00 (s, 1H), 5.40 (dd, J = 1, 10.5 Hz, 1H), 5.64 (dd, J = 1, 17 Hz, 1H), 6.38 (dd, J = 10.5, 17 Hz, 1H), 7.77 and 8.22 (ABq, J = 9 Hz, 4H); ^{13}C NMR 54.0, 78.2, 116.9, 123.5, 127.3, 137.0, 147.6, 147.8, 173.4; IR (neat) 1737 cm^{-1}. Anal. Calcd for $C_{11}H_{11}NO_5$: C, 55.70; H, 4.67; N, 5.90. Found: C, 55.72; H, 4.71; N, 5.76.

Acknowledgment. This work was made possible through a grant from the National Science Foundation (CHE 9004980).

Supporting Information Available: ^{1}H NMR spectra for **8a**, **11**, **13**, **15**, and **16** and the ^{13}C NMR spectrum of **14** (6 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO960477M