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Selective Amination Reactions of α-Nitro Aryl and Heteroaryl Enoates

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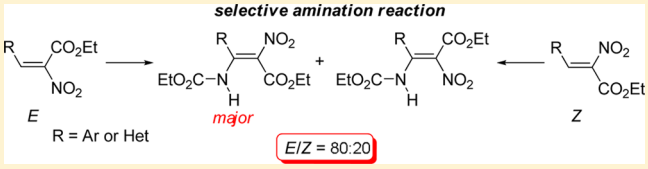
Supporting Information

ABSTRACT: Highly functionalized tetrasubstituted alkenes were obtained by an unexpected amination reaction promoted by ethyl nosyloxycarbamate on various α-nitro aryl and heteroaryl enoates. A nitrene is likely the aminating species responsible for the observed insertion reaction leading to (*E*)-β-amino α-nitro enoates as the major products, regardless of the substrate configuration. The compounds, bearing two nitrogenous functional groups in different oxidation states, can be regarded as interesting synthons. In contrast, aziridination was observed for α-nitro alkyl enoates or β-nitro allylic alcohols.



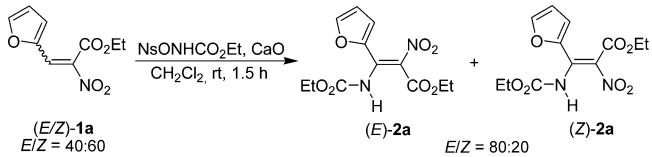
The versatility of the nitro group, often called a "chemical chameleon",[1] as a precursor of various functionalities makes nitro alkenes attractive starting materials to obtain variously functionalized nitro alkanes, compounds in which the nitro group can be transformed into various useful functional groups.[2−6] Because of the significance of nitro alkenes in organic synthesis, some methodologies have been developed giving multifunctionalized structures by modifying both the classical Henry addition/β-elimination procedure[7] and using the Morita−Baylis−Hillman condensation.[8] Nitro alkenes are among the most important Michael acceptors because of the strong electron-withdrawing capacity of the nitro group.[9,10] Efficient access to adjacent quaternary and tertiary stereocenters can be achieved through addition of substituted cyclic or acyclic β-keto esters, α-cyano acetate, and dimethyl malonate nucleophiles to nitro alkenes bearing aryl, heteroaryl, and alkyl groups.[11] Also, nitrogen nucleophiles, such as aza-anions derived from alkyl nosyloxycarbamates ($NsONHCO_2R$; Ns = 4-$NO_2C_6H_4SO_2$), gave, under heterogeneous conditions, aza-Michael additions, followed by ring-closure reactions to variously alkyl or aryl substituted nitro alkenes, leading to the corresponding functionalized nitro aziridines.[12,13] These latter compounds are intriguing precursors of various aminated compounds as well as of more complex heterocyclic compounds.

Recently, starting from conjugated dinitro dienes, a highly stereoselective synthesis of (±)-bis(nitroaziridines) was reported by us.[14] The aziridination reactions led to the expected compounds in very good yields, but, surprisingly, only starting from alkyl substituted nitro alkenes. On the contrary, the reactions were unsuccessful starting from dinitro dienes bearing aryl groups.

Interested in these results and with the aim of obtaining further data on the amination outcome of aryl nitro alkenes, we decided to investigate the reactivity of various *gem*-disubstituted aryl nitro alkenes, such as α-nitro cinnamates and hetero analogues, which are versatile building blocks widely used in organic synthesis as good Michael acceptors. Thus, following the domino synthetic procedure reported by us,[15] some aryl and heteroaryl α-nitro enoates were synthesized and then tested in the amination reactions via carbamate to obtain precursors of amino acids,[16] bearing two nitrogenous functional groups in different oxidation states in the same structure.

The amination with ethyl nosyloxycarbamate ($NsONHCO_2Et$) was attempted on (*E*/*Z*)-**1a**; however, even when some reaction conditions, such as temperatures (0 °C, rt, 40 °C), solvents (CH_2Cl_2 or THF), concentrations, molar ratios, and/or inorganic bases (CaO or NaH), were changed, complex crude mixtures were obtained in all cases. The ^1H NMR analysis always showed after ca. 1.5 h substrate signal disappearance along with the appearance of two singlets around 9.65 (major) and 9.87 ppm, as the only clear new signals. The best reaction conditions were fixed by using a molar ratio of **1a**/CaO/$NsONHCO_2Et$ = 1:3:1.5 in CH_2Cl_2 at room temperature with stirring for 1 h. After purification by flash chromatography, the multifunctionalized isomers (**2a**) were isolated, as the only amination products (Scheme 1).

Scheme 1. Amination Reaction of *E*/*Z* Mixture of Nitro Enoates 1a



Furthermore, the stereochemical reaction outcome appeared quite intriguing. In fact, starting from a 40:60 *E*/*Z* mixture of **1a**, the corresponding *E*/*Z* mixture of **2a** was obtained with a diastereomeric ratio of *E*/*Z* = 80:20, as determined from ^1H NMR spectra obtained from the crude mixture, suggesting that the amination reaction takes place through an intermediate in

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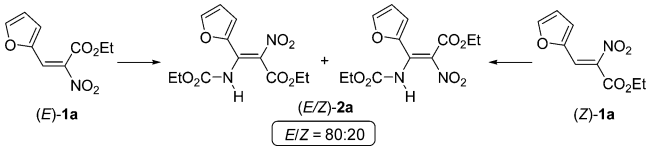
which the configuration of the starting (*E*)-alkene was partially lost.

Interested in the obtained results, we decided to repeat the amination reaction starting from pure α-nitro enoates (*E*)-**1a** and (*Z*)-**1a**, with the hope of getting more insight on the stereochemical outcome. Unexpectedly, the same diastereomeric ratio (80:20) of (*E*/*Z*)-**2a** was obtained, starting from either pure (*E*)- or pure (*Z*)-alkene (Scheme 2).

Scheme 2. Amination Reactions of Pure (*E*)- and (*Z*)-Nitro Enoates 1a



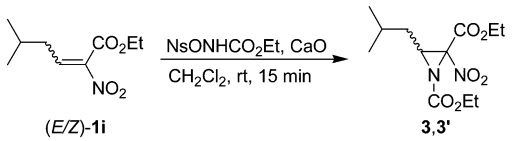
Next, we considered the amination reactions of the (*E*/*Z*)-α-nitro enoates **1b**−**1h** in order to study the reproducibility of the observed amination pathway and stereochemical outcome and so gain further data useful to explain the reaction of **1a**. The results are reported in Table 1.

In all cases, the β-amino α-nitro enoates (*E*/*Z*)-**2** were obtained as the only amination products after flash chromatography on silica gel, although in moderate yields, probably due to loss during the purification process, and no starting material was recovered. The most interesting data is the stereoselectivity of the reactions. Surprisingly, ^{1}H NMR analyses of the crude mixtures clearly showed the same stereochemical results starting both from various nitro alkenes and even from mixtures of them. In fact, compounds **2** were always obtained with an *E*/*Z* ratio = 80:20. Also, when the aminations were performed starting from pure isomers (entries 9−12), the reactions proceeded by a two-step process involving an intermediate in which the free rotation around the single C−C bond is permitted under thermodynamic control.

On the basis of these data, the amination reaction was attempted under heterogeneous conditions ($NsONHCO_2Et$/CaO/CH_2Cl_2) on the alkyl analogue (*E*/*Z*)-**1i**,[15] in order to study the influence of the β-substituent on the amination reaction pathway.

After only a few minutes, NMR analyses performed on the crude mixture showed a completely different outcome for this reaction, (*E*/*Z*)-**1i** being quantitatively converted into the corresponding diastereomeric aziridines **3**,**3**′ (95% yield) that were formed as usual by a reaction via aza-anion[12,13] in a diastereomeric ratio (dr) very similar to that of the starting alkenes (Scheme 3). The result could suggest that the observed

Scheme 3. Aziridination of *E*/*Z* Mixture of Nitro Enoates 1i with $NsONHCO_2Et$



(*E*/*Z*)-**2** may result from unstable and not isolable aryl substituted aziridines by a successive rearrangement reaction. To test this hypothesis, aziridines **3**,**3**′ were stirred in the presence of CaO, either at room temperature or at 40 °C, also for long times, but in all cases, they were almost completely recovered in the same diastereomeric ratio, thus indicating a certain stability for these heterocyclic compounds.

If the hypothesis outlined above can be excluded, tetrasubstituted alkenes **2** may be formed through an unexpected regioselective attack of (ethoxycarbonyl)nitrene (NCO_2Et),[17] formed in situ by an α-elimination reaction of the corresponding aza-anion ($NsON^-CO_2Et$). To gain more insight,[18] *tert*-butyl nosyloxycarbamate (NsONHBoc) was considered as a useful reagent because it is known[19,20] to give alkene aziridination reactions only through the aza-anion pathway,[21] the corresponding nitrene being not formed. The aminations were separately attempted on nitro alkenes **1a** and **1i** carefully under the same reaction conditions and also while changing some reaction parameters (molar ratios, reaction time, concentration). Starting from **1i**, *N*-Boc-protected aziridines **4**,**4**′ were obtained in very high yields (95%) under the usual conditions (Scheme 4), while all attempts to aminate **1a** failed, the unreacted substrate being always recovered.[22]

Scheme 4. Aziridination of *E*/*Z* Mixture of Nitro Enoates 1i with NsONHBoc

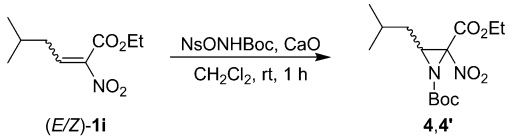
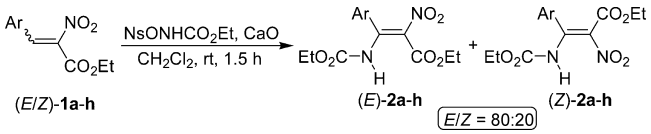
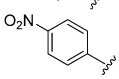
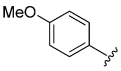


Table 1. Amination Reactions of the (*E*/*Z*)-α-Nitro Enoates[a,b,c,d]



Entry	1	Ar	*E*/*Z* molar ratio of 1	2	Yield[a] (%)
1			40:60		30
2	**a**		0:100[b]	**a**	29
3			100:0[b]		32
4	**b**		30:70	**b**	21
5	**c**		40:60	**c**	24
6	**d**		40:60	**d**	27
7	**e**		40:60	**e**	24
8			40:60		32
9	**f**		0:100[c]	**f**	27
10			100:0[c]		25
11			0:100[d]		23
12	**g**		100:0[d]	**g**	22
13	**h**		45:55	**h**	27

[a]Overall yields in the amination products after flash chromatography on silica gel. For the yields of each isomer, see the Experimental Section. [b]Purified by flash chromatography on silica gel (eluent hexane/ethyl acetate = 4:6). [c]Purified by flash chromatography on silica gel (eluent hexane/ethyl acetate = 8:2). [d]Purified by flash chromatography on silica gel (eluent hexane/ethyl acetate = 1:1).

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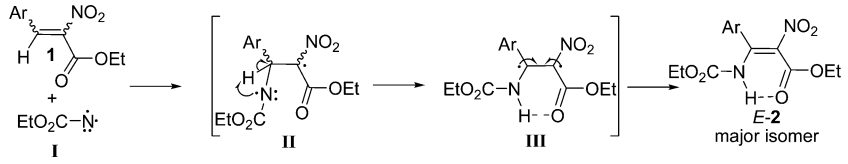
Scheme 5. Possible Pathway for the Synthesis of 2



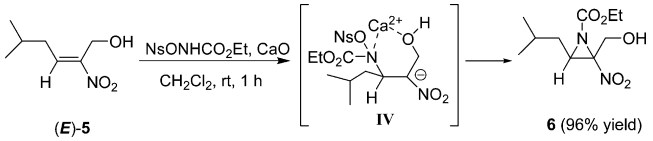
The results seem to support the hypothesis that the synthesis of (*E*/*Z*)-**2** involves NCO_2Et as an aminating agent, in contrast to the possibility that these compounds can derive from an aza-MIRC (Michael Initiated Ring Closure)[12] reaction, followed by the isomerization of highly unstable aziridine intermediates.

A possible reaction pathway involving a two-step reaction of (ethoxycarbonyl)nitrene on aryl substituted **1** is proposed to explain the stereochemical course of the amination reactions (Scheme 5).

It is possible that the obtained tetrasubstituted alkenes **2** derive from the involvement of a triplet species (**I**). In the intermediate **II**, the hydrogen abstraction reaction[23] might be much faster than the ring-closure reaction, leading to the vicinal diradical species **III**, that mainly collapses after rotation around the C−C single bond. In this way, major products were (*E*)-vinyl carbamates, further stabilized by an intramolecular hydrogen bond with the carbonyl group that, as is well-known, forms hydrogen bonds stronger than a nitro group.[24,25]

Considering the possibility that the observed reaction outcome may be due to the effect of the presence of two geminal electron-withdrawing groups on the double bond, the amination reactions with $NsONHCO_2Et$ were performed on (*E*)-2-nitro allylic alcohols bearing various aryl or heteroaryl substituents (Ph, *p*-$NO_2C_6H_4$, *p*-OMe-C_6H_4, 2-furyl). No amination reactions were observed even after long reaction times (72 h) and independently from the nature of the considered aryl residue. On the contrary, (*E*)-2-nitro allylic alcohol **5** was quantitatively converted into the corresponding aziridine **6**, so showing the effectiveness of the aza-MIRC reactions via carbamates even in the presence of a hydroxy group (Scheme 6).

Scheme 6. Aziridination of 2-Nitro Allylic Alcohol (*E*)-5



As expected,[26] aziridine **6** was formed with total retention of the alkene configuration, possibly due to the formation of the intermediate complex **IV** in which the rotation around the C−C single bond was inhibited.

These last results clearly show the influence of the ester moiety on the amination of α-nitro enoates. The presence of the ester group in the geminal position with respect to the nitro group seems to modify the double bond polarization, thus allowing formation of β-amino α-nitro enoates.

In conclusion, the synthesis of highly functionalized tetrasubstituted alkenes characterized by the presence of two nitrogenous functional groups in different oxidation states of α- and β-positions was reported. The aminations most likely involved a nitrene species that gave a formal regioselective insertion reaction only on the benzyl C−H bonds, leading to (*E*)-β-amino α-nitro enoates with good stereoselectivity, regardless of the substrate configuration. It is well-known that tetrasubstituted alkenes are very interesting compounds in organic chemistry, often difficult to synthesize.[27−32] Compounds with structures similar to those reported here were rarely present in the literature, as patents, and showed insecticidal properties.[33−35] In addition, obtained β-amino α-nitro enoates can be regarded as interesting synthons.[36]

EXPERIMENTAL SECTION

IR spectra were recorded on an FT/IR spectrophotometer in $CHCl_3$ as the solvent. ^1H NMR and ^{13}C NMR spectra were recorded by a 300 MHz NMR spectrometer. $CDCl_3$ was used as the solvent and $CHCl_3$ as the internal standard. HRMS analyses were performed using a quadrupole time-of-flight (TOF) mass spectrometer equipped with an ESI source and a syringe pump. The experiments were conducted in the positive ion mode. $NsONHCO_2Et$,[37] NsONHBoc,[20,38] and α-nitro enoates **1a−1h**[15] were synthesized according to literature procedures.

Amination Reactions of Nitro Alkenes 1a−1g. General Procedure. To a stirred CH_2Cl_2 (4 mL) solution of (*E*,*Z*)-**1** (1 mmol) were added CaO (3 mmol) and NsONHBoc (1.5 mmol) at room temperature. After the reactions were complete (TLC), hexane was added, the crude mixtures were filtered, and the solvents were removed in vacuo. The diastereomeric crude mixtures were purified by flash chromatography on silica gel.

Synthesis of (*Z*)- and (*E*)-2a. Overall yield: 30%, from an (*E*/*Z*)-alkene mixture, 29% from (*Z*)-alkene, 32% from (*E*)-alkene. Purified by flash chromatography on silica gel (eluent: hexane/ethyl acetate = 7:3); ν_{max} 3559, 3288, 1759, 1736, 1688, 1536 cm^{-1}.

Ethyl (2*Z*)-3-[(Ethoxycarbonyl)amino]-3-(furan-2-yl)-2-nitroprop-2-enoate. (Orange oil, 18.6 mg from (*E*)-alkene): ^1H NMR δ 1.20 (t, *J* = 7.1 Hz, 3H), 1.25 (t, *J* = 7.1 Hz, 3H), 4.20 (q, *J* = 7.1 Hz, 2H), 4.30 (q, *J* = 7.1 Hz, 2H), 6.54 (dd, *J* = 3.6 Hz, 1.7 Hz, 1H), 6.87 (dd, *J* = 3.5 Hz, 0.7 Hz, 1H), 7.63 (dd, *J* = 1.7 Hz, 0.7 Hz, 1H), 9.87 (br, 1H); ^{13}C NMR δ 13.7, 14.0, 62.5, 62.7, 112.2 (2C), 117.3, 137.4, 142.2, 146.4, 151.0, 160.5; HRMS (ESI-QToF) *m*/*z* calcd for $C_{12}H_{14}N_2NaO_7$ $[M + Na]^+$ 321.0699, found 321.0691.

Ethyl (2*E*)-3-[(Ethoxycarbonyl)amino]-3-(furan-2-yl)-2-nitroprop-2-enoate. (Orange oil, 74.0 mg from (*E*)-alkene): ^1H NMR δ 1.26 (t, *J* = 7.1 Hz, 3H); 1.33 (t, *J* = 7.1 Hz, 3H); 4.16 (q, *J* = 7.1 Hz, 2H, CH_2); 4.34 (q, *J* = 7.1 Hz, 2H); 6.51 (dd, *J* = 3.6 Hz, 1.8 Hz, 1H); 6.82 (dd, *J* = 3.6 Hz, 0.7 Hz, 1H) 7.59 (dd, *J* = 1.8 Hz, 0.7 Hz, 1H); 9.65 (br, 1H); ^{13}C NMR δ 13.9; 14.1; 62.7; 62.8; 112.4 (2C); 116.6; 139.1; 141.4; 146.0; 151.7; 161.7; HRMS (ESI-QToF) *m*/*z* calcd for $C_{12}H_{14}N_2NaO_7$ $[M + Na]^+$ 321.0699, found 321.0703.

Synthesis of (*Z*)- and (*E*)-2b. Overall yield: 21% (62.6 mg). Purified by flash chromatography on silica gel (eluent: hexane/ethyl acetate = 8:2); ν_{max} 3565, 3249, 1758, 1739, 1688, 1536 cm^{-1}. *Ethyl (2Z)-3-[(ethoxycarbonyl)amino]-3-(furan-3-yl)-2-nitroprop-2-enoate* (brown oil, 12.5 mg): ^1H NMR δ 1.15 (t, *J* = 7.1 Hz, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 4.19 (q, *J* = 7.1 Hz, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 6.51−6.52 (m, 1H), 7.48−7.49 (m, 1H), 7.63−7.64 (m, 1H), 10.59 (br, 1H); ^{13}C NMR δ 13.5, 14.1, 62.7, 63.2, 111.3, 124.2, 131.0, 143.4, 143.6, 143.8, 151.7, 162.1; HRMS (ESI-QToF) *m*/*z* calcd for $C_{12}H_{14}N_2NaO_7$ $[M + Na]^+$ 321.0699, found 321.0690. *Ethyl (2E)-3-[(ethoxycarbonyl)amino]-3-(furan-3-yl)-2-nitroprop-2-enoate* (brown oil, 50.0 mg): ^1H NMR δ 1.26 (t, *J* = 7.1 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H), 4.15 (q, *J* = 7.1 Hz, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 6.46−6.47 (m, 1H), 7.45−7.46 (m, 1H), 7.60−7.63 (m, 1H), 10.16 (br, 1H); ^{13}C NMR δ 14.0 (2C), 62.6; 62.8; 110.8, 124.4, 129.1, 143.1, 143.3, 143.8, 151.5,

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162.0; HRMS (ESI-QToF) m/z calcd for $C_{12}H_{14}N_2NaO_7$ $[M + Na]^+$ 321.0699, found 321.0693.

Synthesis of (*Z*)- and (*E*)-2c. Overall yield: 24% (74.5 mg). Purified by flash chromatography on silica gel (eluent: hexane/ethyl acetate = 7:3); ν_{max} 3566, 3268, 1754, 1733, 1684, 1535 cm^{-1}. *Ethyl (2Z)-3-[(ethoxycarbonyl)amino]-2-nitro-3-(thiophen-2-yl)prop-2-enoate* (brown oil, 15.1 mg): ^1H NMR δ 1.26 (t, J = 7.0 Hz, 3H), 1.33 (t, J = 7.0 Hz, 3H), 4.17 (q, J = 7.0 Hz, 2H), 4.34 (q, J = 7.0 Hz, 2H), 7.06−7.09 (m, 1H), 7.28−7.30 (m, 1H), 7.62−7.64 (m, 1H), 10.26 (br, 1H); ^{13}C NMR δ 13.9, 14.1, 62.2; 63.3, 115.1, 127.2, 130.6, 131.2, 131.4, 144.5, 151.9, 160.5; HRMS (ESI-QToF) m/z calcd for $C_{12}H_{14}N_2NaO_6S$ $[M + Na]^+$ 337.0457, found 337.0463. *Ethyl (2E)-3-[(ethoxycarbonyl)amino]-2-nitro-3-(thiophen-2-yl)prop-2-enoate* (brown oil, 60.3 mg): ^1H NMR δ 1.23 (t, J = 7.0 Hz, 3H), 1.35 (t, J = 7.0 Hz, 3H), 4.12 (q, J = 7.0 Hz, 2H), 4.31 (q, J = 7.0 Hz, 2H), 7.04−7.07 (m, 1H), 7.24−7.26 (m, 1H), 7.59 (dd, J = 5.0 Hz, 1.1 Hz, 1H), 9.98 (br, 1H); ^{13}C NMR δ 14.0, 14.1, 62.7, 62.8, 115.4, 127.4, 130.6, 131.1, 131.4, 144.5, 151.8, 161.7; HRMS (ESI-QToF) m/z calcd for $C_{12}H_{14}N_2NaO_6S$ $[M + Na]^+$ 337.0457, found 337.0464.

Synthesis of (*Z*)- and (*E*)-2d. Overall yield: 27% (83.2 mg). Purified by flash chromatography on silica gel (eluent: hexane/ethyl acetate = 8:2); ν_{max} 3566, 3268, 1754, 1733, 1684, 1535 cm^{-1}. *Ethyl (2Z)-3-[(ethoxycarbonyl)amino]-2-nitro-3-phenylprop-2-enoate* (yellow oil, 16.6 mg): ^1H NMR δ 1.10 (t, J = 7.1 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H), 4.12 (q, J = 7.1 Hz, 2H), 4.34 (q, J = 7.1 Hz, 2H), 7.26−7.65 (m, 5H), 10.66 (br, 1H); ^{13}C NMR δ 14.2, 14.3, 62.8, 63.9, 112.0, 127.7, 128.2, 128.6 (2C), 129.5, 130.8, 148.8, 153.4, 162.5; HRMS (ESI-QToF) m/z calcd for $C_{14}H_{16}N_2NaO_6$ $[M + Na]^+$ 331.0906, found 331.0897. *Ethyl (2E)-3-[(ethoxycarbonyl)amino]-2-nitro-3-phenylprop-2-enoate* (yellow oil, 66.5 mg): ^1H NMR δ 1.20 (t, J = 7.1 Hz, 3H), 1.34 (t, J = 7.1 Hz, 3H), 4.07 (q, J = 7.1 Hz, 2H), 4.35 (q, J = 7.1 Hz, 2H), 7.27−7.72 (m, 5H), 10.30 (br, 1H); ^{13}C NMR δ 14.3 (2C), 62.6, 63.4, 111.8, 127.6, 128.0, 128.4 (2C), 129.2, 130.9, 147.9, 152.0, 160.6; HRMS (ESI-QToF) m/z calcd for $C_{14}H_{16}N_2NaO_6$ $[M + Na]^+$ 331.0906, found 331.0911.

Synthesis of (*Z*)- and (*E*)-2e. Overall yield: 24% (78.2 mg). Purified by flash chromatography on silica gel (eluent: hexane/ethyl acetate = 8:2); ν_{max} 3565, 3262, 1761, 1734, 1686, 1542 cm^{-1}. *Ethyl (2Z)-3-[(ethoxycarbonyl)amino]-2-nitro-3-(4-fluorophenyl)prop-2-enoate* (dark yellow oil, 15.6 mg): ^1H NMR δ 1.11 (t, J = 7.1 Hz, 3H), 1.25 (t, J = 7.1 Hz, 3H), 4.13 (q, J = 7.1 Hz, 2H), 4.35 (q, J = 7.1 Hz, 2H), 7.07−7.13 (m, 2H), 7.32−7.36 (m, 2H), 10.63 (br, 1H); ^{13}C NMR δ 13.5, 13.9, 62.5, 63.0, 113.5, 115.7, 124.4 (2C), 130.3, 130.4, 131.0, 151.6, 162.3, 165.6; HRMS (ESI-QToF) m/z calcd for $C_{14}H_{15}FN_2NaO_6$ $[M + Na]^+$ 349.0812, found 349.0820. *Ethyl (2E)-3-[(ethoxycarbonyl)amino]-2-nitro-3-(4-fluorophenyl)prop-2-enoate* (dark yellow oil, 62.6 mg): ^1H NMR δ 1.22 (t, J = 7.1 Hz, 3H), 1.33 (t, J = 7.1 Hz, 3H), 4.09 (q, J = 7.1 Hz, 2H), 4.37 (q, J = 7.1 Hz, 2H), 7.05−7.11 (m, 2H), 7.32−7.37 (m, 2H), 10.29 (br, 1H); ^{13}C NMR δ 13.8, 14.0, 62.6, 62.7, 113.6, 115.9, 124.2, 125.4, 129.6, 129.8, 131.1, 150.7, 162.1, 165.5; HRMS (ESI-QToF) m/z calcd for $C_{14}H_{15}FN_2NaO_6$ $[M + Na]^+$ 349.0812, found 349.0796.

Synthesis of (*Z*)- and (*E*)-2f. Overall yield: 32%, from an (*E*/*Z*)-alkene mixture, 27% from (*Z*)-alkene, 25% from (*E*)-alkene. Purified by flash chromatography on silica gel (eluent: hexane/ethyl acetate = 8:2); ν_{max} 3566, 3265, 1754, 1737, 1689, 1534 cm^{-1}. *Ethyl (2Z)-3-[(ethoxycarbonyl)amino]-2-nitro-3-(4-nitrophenyl)prop-2-enoate* (orange oil, 22.6 mg from an (*E*/*Z*)-alkene mixture): ^1H NMR δ 1.26 (t, J = 7.1 Hz, 3H), 1.37 (t, J = 7.1 Hz, 3H), 4.13 (q, J = 7.1 Hz, 2H), 4.38 (q, J = 7.1 Hz, 2H), 7.56−7.62 (m, 2H), 8.24−8.31 (m, 2H), 1.60 (br, 1H); ^{13}C NMR δ 13.5, 14.0, 62.8, 63.6, 112.3, 123.3, 124.3, 129.4 (2C), 135.8, 148.9, 149.1, 151.6, 162.4; HRMS (ESI-QToF) m/z calcd for $C_{14}H_{15}N_3NaO_8$ $[M + Na]^+$ 376.0757, found 376.0745. *Ethyl (2E)-3-[(ethoxycarbonyl)amino]-2-nitro-3-(4-nitrophenyl)prop-2-enoate* (orange oil, 90.4 mg from an (*E*/*Z*)-alkene mixture): ^1H NMR δ 1.23 (t, J = 7.1 Hz, 3H), 1.35 (t, J = 7.1 Hz, 3H), 4.09 (q, J = 7.1 Hz, 2H), 4.38 (q, J = 7.1 Hz, 2H), 7.51−7.56 (m, 2H), 8.23−8.30 (m, 2H), 10.36 (br, 1H); ^{13}C NMR δ 13.9, 14.1, 63.0, 63.1, 111.9, 123.6, 124.0, 128.8 (2C), 136.0, 148.7, 149.1, 151.5, 161.9; HRMS (ESI-QToF) m/z calcd for $C_{14}H_{15}N_3NaO_8$ $[M + Na]^+$ 376.0757, found 376.0763.

Synthesis of (*Z*)- and (*E*)-2g. Overall yield: 23% from (*Z*)-alkene, 22% from (*E*)-alkene. Purified by flash chromatography on silica gel (eluent: hexane/ethyl acetate = 8:2); ν_{max} 3545, 3264, 1761, 1737, 1684, 1534 cm^{-1}. *Ethyl (2Z)-3-[(ethoxycarbonyl)amino]-2-nitro-3-(4-methoxyphenyl)prop-2-enoate* (pale yellow oil, 15.5 mg from (*Z*)-alkene): ^1H NMR δ 1.25 (t, J = 7.1 Hz, 3H), 1.33 (t, J = 7.1 Hz, 3H), 3.83 (s, 3H), 4.13 (q, J = 7.1 Hz, 2H), 4.34 (q, J = 7.1 Hz, 2H), 7.02−7.08 (m, 2H), 7.31−7.36 (m, 2H), 10.60 (br, 1H); ^{13}C NMR δ 13.5, 14.3, 55.3, 62.3, 63.0, 113.8, 121.9, 129.2 (2C), 129.8 (2C), 150.0, 151.1, 161.7, 163.0; HRMS (ESI-QToF) m/z calcd for $C_{15}H_{19}N_2O_7$ $[M + H]^+$ 339.1192, found 339.1183. *Ethyl (2E)-3-[(ethoxycarbonyl)-amino]-2-nitro-3-(4-methoxyphenyl)prop-2-enoate* (pale yellow oil, 62.2 mg from (*Z*)-alkene): ^1H NMR δ 1.22 (t, J = 7.1 Hz, 4H), 1.31 (t, J = 7.1 Hz, 3H), 3.81 (s, 3H), 4.09 (q, J = 7.1 Hz, 2H), 4.36 (q, J = 7.1 Hz, 4H), 6.94−7.04 (m, 2H), 7.26−7.31 (m, 2H), 10.23 (br, 1H); ^{13}C NMR δ 14.0, 14.1, 55.2, 62.4, 62.6, 113.9, 121.6, 129.1 (2C), 129.6 (2C), 150.3, 151.8, 161.5, 162.2; HRMS (ESI-QToF) m/z calcd for $C_{15}H_{19}N_2O_7$ $[M + H]^+$ 339.1192, found 339.1201.

Synthesis of (*Z*)- and (*E*)-2h. Overall Yield: 27% (96.6 mg). Purified by flash chromatography on silica gel (eluent: hexane/ethyl acetate = 7:3); ν_{max} 3559, 3244, 1755, 1738, 1689, 1551 cm^{-1}. *Ethyl (2Z)-3-[(ethoxycarbonyl)amino]-2-nitro-3-(naphthalen-1-yl)prop-2-enoate* (brown oil, 19.3 mg): ^1H NMR δ 1.02 (t, J = 7.1 Hz, 3H), 1.26 (t, J = 7.1 Hz, 3H), 4.10 (q, J = 7.1 Hz, 2H), 4.38 (q, J = 7.1 Hz, 2H), 7.41−7.53 (m, 2H), 7.61−7.69 (m, 2H), 7.86−7.96 (m, 2H), 8.11−8.15 (m, 1H), 10.64 (br, 1H); ^{13}C NMR δ 13.3, 14.1, 62.0, 63.1, 111.5, 124.7, 124.9, 126.3, 127.1, 128.5, 128.7, 131.3, 133.3, 135.9, 136.4, 147.9, 157.8, 161.6; HRMS (ESI-QToF) m/z calcd for $C_{18}H_{18}N_2NaO_6$ $[M + Na]^+$ 381.1063, found 381.1071. *Ethyl (2E)-3-[(ethoxycarbonyl)-amino]-2-nitro-3-(naphthalen-1-yl)prop-2-enoate* (brown oil, 77.3 mg): ^1H NMR δ 1.05 (t, J = 7.1 Hz, 3H), 1.24 (t, J = 7.1 Hz, 3H), 4.10 (q, J = 7.1 Hz, 2H), 4.39 (q, J = 7.1 Hz, 2H), 7.42−7.55 (m, 2H), 7.61−7.70 (m, 2H), 7.84−7.95 (m, 2H), 8.19−8.23 (m, 1H); 10.37 (br, 1H); ^{13}C NMR δ 13.4, 14.0, 62.6, 63.0, 111.7, 124.8, 125.0, 126.8, 127.1, 128.4, 128.6, 131.3, 133.1, 135.1, 136.2, 147.9, 157.7, 161.7; HRMS (ESI-QToF) m/z calcd for $C_{18}H_{18}N_2NaO_6$ $[M + Na]^+$ 381.1063, found 381.1059.

Synthesis of Aziridines 3,3′. To a stirred CH_2Cl_2 (4 mL) solution of (*E*,*Z*)-**1i** (1 mmol) were added CaO (3 mmol) and $NsONHCO_2Et$ (1.5 mmol) at room temperature. When the reaction was complete (15 min), hexane was added and the crude mixture was filtered and, after evaporation of solvents in vacuo, purified by flash chromatography on silica gel to give pure **3** and **3′**. Overall yield: 276.5 mg, 96%. *Diethyl (2R*,3R*)-3-(2-methylpropyl)-2-nitroaziridine-1,2-dicarboxylate* (**3**) (pale yellow oil, 179.7 mg, 65%) ν_{max} 1757, 1567, 1538 cm^{-1}; ^1H NMR δ 1.02 (d, J = 6.7 Hz, 6H), 1.28 (t, J = 7.1 Hz, 3H), 1.33 (t, J = 7.2 Hz, 3H), 1.52−1.61 (m, 1H), 1.84−1.97 (m, 2H), 3.42 (dd, J = 3.9 Hz, 8.9 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 4.41 (q, J = 7.2 Hz, 2H); ^{13}C NMRδ 13.8, 14.1, 22.0, 22.1, 26.5, 36.9, 48.5, 63.8, 64.4, 89.7, 156.6, 161.1; HRMS (ESI-QToF) m/z calcd for $C_{12}H_{20}N_2NaO_6$ $[M + Na]^+$, 311.1219 found 311.1234. *Diethyl (2R*,3S*)-3-(2-methylpropyl)-2-nitroaziridine-1,2-dicarboxylate* (**3′**) (pale yellow oil, 96,8 mg, 35%) ν_{max} 1757; 1567; 1538 cm^{-1}; ^1H NMR δ 1.01 (d, J = 6.7 Hz, 6H), 1.27 (t, J = 7.1 Hz, 3H), 1.37 (t, J = 7.1 Hz, 3H), 1.62−1.71 (m, 1H), 1.84−1.99 (m, 2H), 3.49 (dd, J = 4.7 Hz, 8.2 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 4.41 (q, J = 7.1 Hz, 2H); ^{13}C NMR δ 13.8, 14.0, 22.0, 22.2, 26.6, 36.8, 49.0, 63.5, 63.8, 93.9, 155.9, 159.6; HRMS (ESI-QToF) m/z calcd for $C_{12}H_{20}N_2NaO_6$ $[M + Na]^+$ 311.1219, found 311.1227.

Synthesis of Aziridines 4,4′. To a stirred CH_2Cl_2 (4 mL) solution of (*E*,*Z*)-**1i** (1 mmol) were added CaO (3 mmol) and NsONHBoc (1.5 mmol) at room temperature. When the reaction was complete (1.5 h), hexane was added and the crude mixture was filtered and, after evaporation of solvents in vacuo, purified by flash chromatography on silica gel to give pure **4** and **4′**. Overall yield: 300.2 mg, 95%. *1-tert-Butyl 2-ethyl (2R*,3R*)-3-(2-methylpropyl)-2-nitroaziridine-1,2-dicarboxylate* (**4**) (pale yellow oil, 201.0 mg, 67%) ν_{max} 1756, 1557, 1538 cm^{-1}; ^1H NMR δ 1.02 (d, J = 6.7 Hz, 6H), 1.37 (t, J = 7.1 Hz, 3H), 1.46 (s, 9H), 1.61−1.70 (m, 1H), 1.83−1.97 (m, 2H), 3.49 (dd, J = 4.4 Hz, 8.5 Hz, 1H), 4.33−4.49 (m, 2H); ^{13}C NMR

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δ 13.8, 21.8, 22.1, 26.5, 27.6, 37.0, 48.8, 63.3, 81.2, 89.5, 154.3, 159.8; HRMS (ESI-QToF) *m/z* calcd for $C_{14}H_{24}N_2NaO_6$ $[M + Na]^+$ 339.1532, found 339.1545. *1-tert-Butyl 2-ethyl (2R*,3S*)-3-(2-methylpropyl)-2-nitroaziridine-1,2-dicarboxylate* (**4′**) (pale yellow oil, 99.0 mg, 33%) ν_{max} 1756, 1557, 1538 cm^{-1}; ^1H NMR δ 1.01 (d, *J* = 6.7 Hz, 6H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.46 (s, 9H), 1.50−1.59 (m, 1H), 1.85−1.96 (m, 2H), 3.40 (dd, *J* = 3.7 Hz, 9.1 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H); ^{13}C NMR δ; 13.8, 21.9, 22.1, 26.5, 27.7, 36.8, 48.4, 64.2, 80.9, 103.5, 155.0, 161.2; HRMS (ESI-QToF) *m/z* calcd for $C_{14}H_{24}N_2NaO_6$ $[M + Na]^+$ 339.1532, found 339.1539.

Synthesis of Ethyl 2-(Hydroxymethyl)(2*R,3*R**)-3-(2-methylpropyl)-2-nitroaziridine-1-carboxylate (6).** To a stirred CH_2Cl_2 (3 mL) solution of (*E*)-**5** (1 mmol) were added CaO (3 mmol) and $NsONHCO_2Et$ (1.5 mmol) at room temperature. When the reaction was complete (1 h), hexane was added and the crude mixture was filtered and, after evaporation of solvents in vacuo, purified by flash chromatography on silica gel to give pure **6** as a pale yellow oil (236.2 mg, 96%). ν_{max} 3432, 1732, 1559, 1537 cm^{-1}; ^1H NMR δ 1.00 (d, *J* = 1.3 Hz, 3H), 1.04 (d, *J* = 1.3 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.39−1.69 (m, 2H), 1.80−2.00 (m, 1H), 2.50 (br, 1H), 3.34 (dd, *J* = 7.7 Hz, 5.1 Hz, 1H), 4.10 (d, *J* = 13.8 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 4.40 (d, *J* = 13.8 Hz, 1H); ^{13}C NMR δ 14.2, 22.1, 22.3, 26.8, 36.9, 48.7, 59.8, 63.6, 78.7, 157.0; HRMS (ESI-QToF) *m/z* calcd for $C_{10}H_{18}N_2NaO_5$ $[M + Na]^+$ 269.1113, found 269.1120.

■ ASSOCIATED CONTENT

Supporting Information

^1H and ^{13}C NMR spectra of compounds (*Z*)-**2a−2h** and (*E*)-**2a−2h**, **3**, **3′**, **4**, **4′**, and **6** are reported. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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