



Further studies on vinamidinium salt amine exchange reactions, borohydride reductions, and subsequent transformations

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ABSTRACT

Studies directed at the amine exchange reaction of vinamidinium salts followed by sodium borohydride reduction to secondary and tertiary allylic amines are described. The tertiary allylic amines were alkylated and subjected to base mediated rearrangement to yield a variety of highly functionalized tertiary homoallylic amines.

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1. Introduction

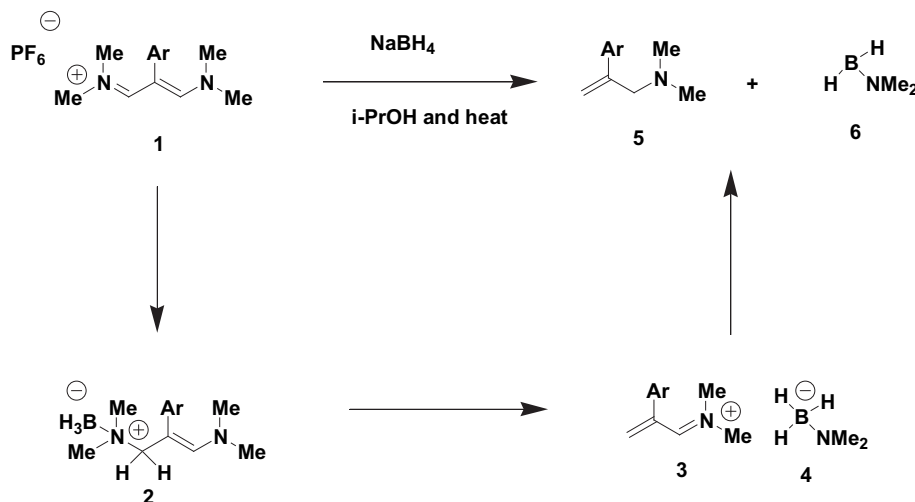
We have previously reported¹ the sodium borohydride reduction of 2-aryl-*N,N,N,N*-tetramethylvinamidinium salts (**1**) to give 2-aryl-3-*N,N*-dimethylaminopropenes (**5**) in good yield. We have suggested that the reaction proceeds according to the steps presented in Scheme 1.

The reduction reaction gives extremely pure 2-aryl-*N,N*-dimethylallylic amines (**5**) from the 2-arylvinamidinium salts (**1**) and the salts themselves are available^{2,3} in good yield from arylacetic acids or arylacetic acid chlorides. Vinamidinium salts function as masked 1,3-dicarbonyl compounds and the 2-substituted systems can be prepared in general from acetic acids or acetic acid chlorides that have electron withdrawing groups or aromatic groups attached at the alpha carbon. Davies³ and his group at Merck have recently prepared such compounds on large scale as a result of their need for significant amounts of a new class of COX-2 inhibitors. Some examples of successful alpha substituents on acetic acids are Cl,⁴ Br,⁴ F,⁴ CF₃,⁵ NO₂,³ phenyl,⁴ substituted phenyl,⁴ naphthyl,⁴ phenylsulfonyl,⁶ benzotriazolyl,⁷ and carboxy.⁴ The isolated yields of

the respective vinamidinium salts are in the range of 60–90% and such salts form very well defined solids and have a very good shelf life. The preparation of these salts is normally accomplished by heating the respective acids under Vilsmeier–Haack conditions with a mixture of DMF and phosphorous oxychloride and quenching the reaction mixture with an aqueous solution of sodium hexafluorophosphate or similar salt. The formation of these salts is presumed to proceed through a ketene⁴ type intermediate and it is thought that electron withdrawing groups and aromatic groups at the 2-position of the acetic acid facilitate ketene formation from the acid chloride precursor. For this reason, yields of 2-alkylvinamidinium salts³ by the indicated procedure are usually quite low. The 1-substituted vinamidinium salts are available⁸ from chloropropenium salts but a large part of our focus has been to examine the reactions of the 2-substituted systems as a consequence of their ready availability and the often unique properties⁶ imparted by location of a particular substituent at the 2 position.

Allylic amines are known to be useful reagents⁹ and have functioned as important building blocks in organic chemistry. Some examples involve the cross-linking of proteins,¹⁰ rhodium catalyzed ylide formation,¹¹ directed metalation reactions¹² and the preparation of GABA uptake inhibitors.¹³ The quaternary salts derived from such amines can function as useful alkylating agents^{14,15} for

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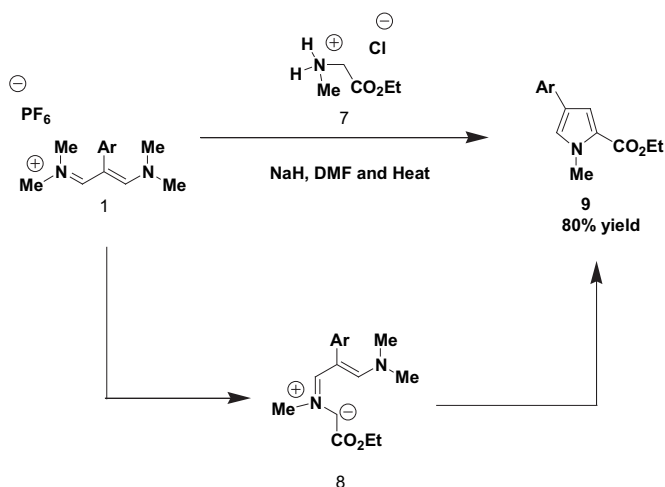


Scheme 1. Sodium borohydride reduction of vinamidinium salts.

a variety of nucleophilic species and when properly functionalized can undergo base mediated 2,3-sigmatropic rearrangement to give homoallylic amines.¹⁶ Jorgensen⁹ and Johannsen have recently reviewed the preparation of allylic amines and have suggested that the direct approach to such systems involves either (1) nucleophilic substitution of an allylic halide or allylic halide equivalent with an amine or (2) direct allylic amination of alkenes. The allylic substitution reaction occasionally suffers from over alkylation processes and there are certainly regiochemical issues associated with direct allylic amination of unsymmetrical alkenes. Since our previously demonstrated reduction chemistry had no such issues, we decided to examine extending the generality of our reduction sequence (Scheme 1) to a variety of tertiary and secondary allylic amine systems and thereby further define the scope and limitation of this methodology.

2. Results and discussions

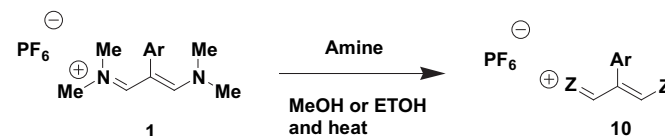
In order to make the conversion of vinamidinium salt to allylic amine of greater utility, it is necessary to have access to vinamidinium salts (**1**) with diverse amine functionality. It is known¹⁷ that vinamidinium salts (**1**) can undergo amine exchange reactions and we have previously used this concept for the preparation of 2,4-disubstitutedpyrroles² (**9**) as depicted in Scheme 2.



Scheme 2. Preparation of 2,4-disubstitutedpyrroles from vinamidinium salts.

With this strategy in mind, we have carried out amine exchange reactions with the parent vinamidinium salt (**1**, Ar=4-methoxyphenyl) with a variety of amines as presented in Table 1. The reaction is carried out by heating excess primary or secondary amines with the parent vinamidinium salt in methanol or ethanol for several hours in which case dimethylamine gas is evolved and the exchange reaction is driven to completion in very high yield with excellent purity. Cyclic secondary amines in addition to acyclic secondary amines work very well in the transformation and primary amine exchanged salts also undergo the process very efficiently. In addition, we have examined several different aromatic substituents on the vinamidinium salts (**10j–m** in Table 1) and such functional group changes do not impact the yield or purity of the amine exchanged products.

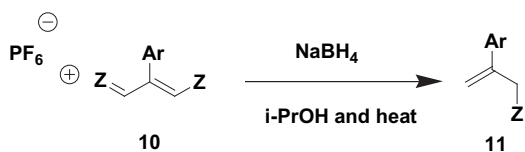
Table 1
Amine exchange reactions of vinamidinium salts



Compound	Amine group (Z)	Ar group	%Yield of exchanged salt (10)
10a	Pyrrolidinyl	4-Methoxyphenyl	99
10b	Morpholinyl	4-Methoxyphenyl	99
10c	Piperidinyl ³	4-Methoxyphenyl	89
10d	Diethylamino	4-Methoxyphenyl	96
10e	Dipropylamino	4-Methoxyphenyl	93
10f	Butylamino	4-Methoxyphenyl	71
10g	Hexylamino	4-Methoxyphenyl	97
10h	s-Butylamino	4-Methoxyphenyl	50
10i	2,4-Dimethoxybenzylamino	4-Methoxyphenyl	50
10j	Butylamino	4-Chlorophenyl	98
10k	Butylamino	3,4-Dimethoxyphenyl	97
10l	Butylamino	4-Methylphenyl	97
10m	Butylamino	1-Naphthyl	97

With a variety of amine exchanged vinamidinium salts in hand, these materials were subjected to sodium borohydride reduction in refluxing isopropanol (Table 2) and the corresponding allylic amines (**11**) were produced in very good yield with excellent purity. It is interesting to note that the primary amine exchanged vinamidinium salts underwent the reduction in an equally efficient

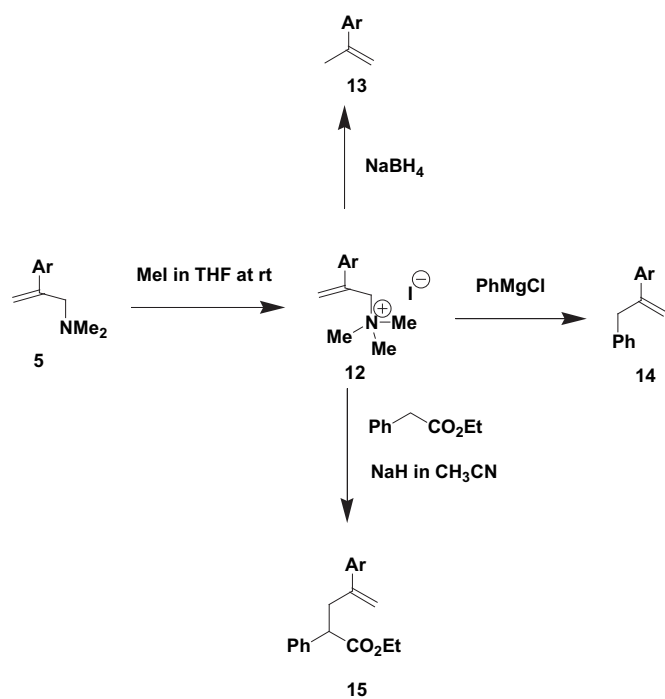
Table 2
Sodium borohydride reduction of amine exchanged vinamidinium salts



Compound	Amine group (Z)	Ar group	%Yield of allylic amine (11)
11a	Pyrrolidinyl	4-Methoxyphenyl	89
11b	Morpholinyl ¹³	4-Methoxyphenyl	97
11c	Piperidinyl	4-Methoxyphenyl	97
11d	Diethylamino	4-Methoxyphenyl	96
11e	Dipropylamino	4-Methoxyphenyl	99
11f	Butylamino	4-Methoxyphenyl	62
11g	Hexylamino	4-Methoxyphenyl	99
11h	<i>s</i> -Butylamino	4-Methoxyphenyl	62
11i	2,4-Dimethoxybenzylamino	4-Methoxyphenyl	60
11j	Butylamino	4-Chlorophenyl	99
11k	Butylamino	3,4-Dimethoxyphenyl	99
11l	Butylamino	4-Methylphenyl	94
11m	Butylamino	1-Naphthyl	98

manner (**11f–m**, Table 2) as did the secondary amine exchanged salts (**11a–e**, Table 2) thereby making such secondary allylic amines available by this route for the first time. The crude products were nearly analytically pure and often utilized in subsequent reactions without additional purification.

As was mentioned earlier, one of the very significant reactions of tertiary allylic amines is conversion to quaternary ammonium salts, which in turn can undergo a variety of useful reactions. We have previously reported such reactions of 2-aryl-*N,N*-dimethylallylic amines (**5**) and these are depicted in Scheme 3. Reduction of the quaternary salts (**12**) to styrenes¹⁴ (**13**), Grignard alkylation to highly functionalized styrenes¹⁴ (**14**) and enolate alkylations to highly functionalized allylic systems¹⁵ (**15**) were accomplished in good yield and in high purity.



Scheme 3. Reaction of quaternary salts with nucleophiles and reducing agents.

Other types of allylic ammonium salts have been carefully studied¹⁶ with regard to base mediated 2,3-sigmatropic rearrangements and we anticipated it would be useful to examine some of our tertiary allylic amines in such an application (Table 3). The pyrrolidine allylic amine (**11a**) was subsequently alkylated with ethyl α -bromoacetate in THF to yield the corresponding quaternary salt (**17a**) in good yield and high purity. This material (**17a**) was fully characterized but, as was the case for all of our salts, the crude product was nearly analytically pure and it was used immediately in the rearrangement step after isolation by solvent removal. All of quaternary salts (**17a–n**) resulting from such alkylations were treated with sodium hydride or sodium *tert*-butoxide in acetonitrile at room temperature and after work up very pure homoallylic products (**18**) were obtained (Table 3). A variety of different aryl group analogs (**18b–g**) were prepared in this manner and it is notable that these compounds represent some uniquely functionalized α -substituted amino acid esters (**18b–g**).

With the indicated results in hand, we assumed that other alkylating agents could be utilized in this sequence if electron withdrawing groups (EWG) were present in the alkylating agent. For example when α -haloacetophenones and nitrobenzyl halides were employed as alkylating agents, uniquely functionalized α -amino ketones (**18j–l**) and α -substituted benzylic amines (**18m–n**) were obtained, respectively, in modest to reasonable yields.

3. Conclusions

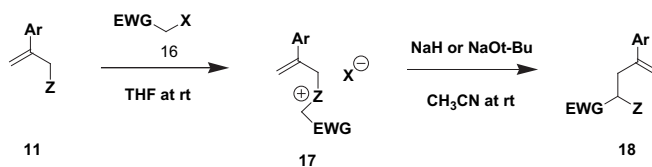
We have described herein a very practical, efficient, and general high yielding preparation of amine exchanged vinamidinium salts (**10**) along with their reduction to the corresponding allylic amines (**11**). Some of the tertiary allylic amines were treated with a variety of electron deficient haloalkane derivatives and under basic conditions the quaternary salts rearranged to uniquely functionalized homoallylic systems (**18**). Such transformations continue to demonstrate the general synthetic utility of vinamidinium salts and their derivatives and offer an alternative to the traditional preparation of highly functionalized allylic amines.

4. Experimental

4.1. General

All chemicals were used as received from the manufacturer (Aldrich Chemicals and Fisher Scientific). All solvents were dried over 4 Å molecular sieves prior to their use. NMR spectra were obtained on either a Bruker 300 MHz spectrometer, a Bruker 500 MHz spectrometer or a Varian Gemini 200 MHz spectrometer in either CDCl₃, DMSO-*d*₆ or acetone-*d*₆ solutions. IR spectra were recorded on a Nicolet Avatar 320 FT-IR spectrometer with an HATR attachment. High resolution mass spectra were provided on a Bio-tof Q electrospray mass spectrometer at the University of Richmond or by the Midwest Center for Mass Spectrometry at the University of Nebraska at Lincoln. Low resolution GC–MS spectra were obtained on a Shimadzu QP 5050 instrument. Melting points and boiling points are uncorrected. Chromatographic separations were carried out on a Harrison Chromatotron (equipped with a silica plate) or Biotage SP-1 instrument (equipped with a silica cartridge) and ethyl acetate/hexane was used as the eluant in both instances. The reaction products were eluted within the range of 6–8 column volumes of eluant with a gradient of 60–80% ethyl acetate in hexane. TLC analyses were conducted on silica plates with hexane/ethyl acetate as the eluant. Vinamidinium salts utilized for the described studies were prepared according to standard procedures.^{2–4} All purified reaction products gave TLC results, GC–MS spectra, and ¹³C NMR spectra consistent with a sample purity of >95%. When the preparation of an analytical sample is

Table 3
Alkylation and rearrangement of tertiary allylic amines



Compound	Amine group (Z)	Ar group	EWG	%Yield of rearranged amine (18)
18a	Pyrrolidinyl	4-Methoxyphenyl	CO ₂ Et	83
18b	Dimethylamino	4-Chlorophenyl	CO ₂ Et	90
18c	Dimethylamino	4-Methoxyphenyl	CO ₂ Et	54
18d	Dimethylamino	4-Bromophenyl	CO ₂ Et	70
18e	Dimethylamino	Phenyl	CO ₂ Et	67
18f	Dimethylamino	3,4-Dimethoxyphenyl	CO ₂ Et	62
18g	Dimethylamino	Naphthyl	CO ₂ Et	72
18h	Piperidinyl	4-Methoxyphenyl	CO ₂ Et	40
18i	Dipropylamino	4-Methoxyphenyl	CO ₂ Et	20
18j	Dimethylamino	4-Methoxyphenyl	4-bromobenzoyl	49
18k	Dimethylamino	4-Methoxyphenyl	Benzoyl	76
18l	Dimethylamino	4-Methoxyphenyl	4-Nitrobenzoyl	82
18m	Dimethylamino	4-Methoxyphenyl	2-Nitrophenyl	21
18n	Dimethylamino	4-Methoxyphenyl	4-Nitrophenyl	53

reported, the crude reaction product was of sufficient purity to be used in subsequent steps without further purification.

4.1.1. 1-(2-(4-Methoxyphenyl)-3-pyrrolidin-1-yl-allylidene)pyrrolidinium hexafluorophosphate (10a). To a 100 mL round bottom flask equipped with a magnetic stirring bar and reflux condenser, was added 4-methoxyphenylvinamidinium salt (**1**, 1.00 g, 2.64 mmol), pyrrolidine (1.12 g, 15.9 mmol), and 40 mL of anhydrous ethanol. The resulting reaction mixture was refluxed for 24 h and then cooled to room temperature at which point a solid precipitated. The solid was vacuum filtered with a Buchner funnel and was washed with 2 × 20 mL of cold ethanol. The resulting material was dried using a Kugelrohr apparatus to give a light yellow solid (1.12 g, 99% yield). The resulting solid exhibited the following physical properties: mp 158–159 °C; ¹H NMR (CDCl₃) δ 1.84 (m, 8H), 2.71 (t, J=6.0 Hz, 4H), 3.82 (t, J=6.0 Hz, 4H), 3.87 (s, 3H), 6.89 (d, J=8.5 Hz, 2H), 7.18 (d, J=8.5 Hz, 2H), 7.79 (s, 2H); ¹³C NMR (CDCl₃) δ 160.1, 133.8, 124.4, 113.8, 113.3, 106.3, 56.5, 55.3, 49.3, 26.0, 23.7; IR (neat) 1572 cm⁻¹; HRMS (ES) *m/z* calcd for C₁₈H₂₅N₂O 285.1961, found 285.1967.

4.1.2. 1-(2-(4-Methoxyphenyl)-3-morpholinoallylidene)morpholin-4-ium hexafluorophosphate (10b). This compound was prepared by the above procedure with the exception that morpholine was used in place of pyrrolidine in which case a 99% yield of a tan solid was obtained. This material exhibited the following physical properties: mp 194–197 °C; ¹H NMR (CDCl₃) δ 2.97 (t, J=5.0 Hz, 4H), 3.45 (t, J=5.0 Hz, 4H), 3.68 (t, J=5.0 Hz, 4H), 3.84 (t, J=5.0 Hz, 4H), 3.87 (s, 3H), 6.98 (d, J=4.0 Hz, 2H), 7.18 (d, J=4.0 Hz, 2H), 7.70 (s, 2H); ¹³C NMR (CDCl₃) δ 163.4, 160.5, 132.0, 123.9, 115.5, 104.8, 67.1, 65.7, 57.2, 55.4, 48.1; IR (neat) 1557 cm⁻¹; HRMS (ES) *m/z* calcd for C₁₈H₂₅N₂O₃ 317.1860, found 317.1876.

4.1.3. 1-(2-(4-Methoxyphenyl)-3-piperidin-1-yl-allylidene)piperidinium hexafluorophosphate (10c). This compound was prepared by the above procedure with the exception that piperidine was used in place of pyrrolidine in which case a 89% yield of a brown solid was obtained. This material exhibited the following physical properties: mp 235–238 °C; ¹H NMR (CDCl₃) δ 1.34 (m, 4H), 1.61 (m, 4H), 1.78 (m, 4H), 2.88 (t, J=6.0 Hz, 4H), 3.59 (t, J=6.0 Hz, 4H), 3.87 (s, 3H), 6.98 (d, J=7.0 Hz, 2H), 7.16 (d, J=7.0 Hz, 2H), 7.60 (s, 2H); ¹³C NMR (CDCl₃) δ 162.6, 160.2, 131.7, 125.0, 115.1, 103.9, 59.2, 55.4, 48.2,

28.8, 25.6, 23.5; IR (neat) 1561 cm⁻¹; HRMS (ES) *m/z* calcd for C₂₀H₂₉N₂O 313.2274, found 313.2296.

4.1.4. N-(3-(Diethylamino)-2-(4-methoxyphenyl)allylidene)-N-ethylethanaminium hexafluorophosphate (10d). This compound was prepared by the above procedure with the exception that diethylamine was used in place of pyrrolidine in which case a 96% yield of an orange solid was obtained. This material exhibited the following physical properties: mp 105–107 °C; ¹H NMR (CDCl₃) δ 0.87 (t, J=7.0 Hz, 6H), 1.33 (t, J=7.0 Hz, 6H), 2.88 (q, J=7.0 Hz, 4H), 3.49 (q, J=7.0 Hz, 4H), 3.87 (s, 3H), 6.95 (d, J=6.5 Hz, 2H), 7.25 (d, J=6.5 Hz, 2H), 7.64 (s, 2H); ¹³C NMR (CDCl₃) δ 163.8, 160.3, 132.2, 124.3, 114.5, 105.0, 55.4, 53.2, 42.9, 14.3 and 13.2; IR (neat) 1570 cm⁻¹; HRMS (ES) *m/z* calcd for C₁₈H₂₉N₂O 289.2274, found 289.2338.

4.1.5. N-(3-(Dipropylamino)-2-(4-methoxyphenyl)allylidene)-N-propylpropan-1-aminium hexafluorophosphate (10e). This compound was prepared by the above procedure with the exception that dipropylamine was used in place of pyrrolidine in which case a 93% yield of a solid was obtained. This material exhibited the following physical properties: mp 95–97 °C; ¹H NMR (CDCl₃) δ 0.45 (t, J=7.5 Hz, 6H), 0.98 (t, J=7.5 Hz, 6H), 1.35 (m, 4H), 1.71 (m, 4H), 2.71 (t, J=7.5 Hz, 4H), 3.41 (t, J=7.5 Hz, 4H), 3.87 (s, 3H), 6.98 (d, J=8.0 Hz, 2H), 7.22 (d, J=8.0 Hz, 2H), 7.65 (s, 2H); ¹³C NMR (CDCl₃) δ 169.2, 160.3, 132.4, 124.1, 114.6, 104.8, 60.5, 55.6, 50.2, 22.2, 21.3, 10.6, and 10.5; IR (neat) 1565 cm⁻¹; HRMS (ES) *m/z* calcd for C₂₂H₃₇N₂O 345.2900, found 345.2960.

4.1.6. N-(3-(Butylamino)-2-(4-methoxyphenyl)allylidene)butan-1-aminium hexafluorophosphate (10f). This compound was prepared by the above procedure with the exception that butylamine was used in place of pyrrolidine in which case a 71% yield of a solid was obtained. This material exhibited the following physical properties: mp 163–165 °C; ¹H NMR (CDCl₃) δ 0.94 (t, J=7.5 Hz, 6H), 1.34 (m, 4H), 1.58 (m, 4H), 3.49 (q, J=7.0 Hz, 4H), 3.89 (s, 3H), 6.11 (br s, 2H), 7.13 (d, J=5.5 Hz, 2H), 7.14 (d, J=5.5 Hz, 2H), 7.96 (d, J=15.0 Hz, 2H); ¹³C NMR (CDCl₃) δ 162.9, 160.7, 131.2, 119.4, 116.6, 107.1, 55.5, 49.6, 32.0, 19.4, and 13.5; IR (neat) 1584 cm⁻¹; HRMS (ES) *m/z* calcd for C₁₈H₂₉N₂O 289.2274, found 289.2301.

4.1.7. N-(3-(Hexylamino)-2-(4-methoxyphenyl)allylidene)hexan-1-aminium hexafluorophosphate (10g). This compound was prepared by the above procedure with the exception that hexylamine was

used in place of pyrrolidine in which case a 97% yield of a solid was obtained. This material exhibited the following physical properties: mp 173–176 °C; ^1H NMR (CDCl_3) δ 0.86 (t, $J=6.6$ Hz, 6H), 1.26 (br s, 12H), 1.58 (t, $J=7.2$ Hz, 4H), 3.44 (t, $J=7.2$ Hz, 4H), 3.83 (s, 3H), 6.40 (br s, 2H), 7.07 (d, $J=9.0$ Hz, 2H), 7.13 (d, $J=9.0$ Hz, 2H), and 7.80 (br s, 2H); ^{13}C NMR (CDCl_3) δ 162.6, 160.6, 131.1, 119.3, 116.5, 107.2, 55.4, 49.9, 31.1, 30.0, 25.8, 22.4, and 13.8; IR (neat) 1602 cm^{-1} ; HRMS (ES) m/z calcd for $\text{C}_{22}\text{H}_{37}\text{N}_2\text{O}$ 345.2900, found 345.2935.

4.1.8. *N*-(3-(*sec*-Butylamino)-2-(4-methoxyphenyl)allylidene)butan-2-aminium hexafluorophosphate (10h). This compound was prepared by the above procedure with the exception that *sec*-butylamine was used in place of pyrrolidine in which case a 50% yield of a solid was obtained after flash chromatography. This material exhibited the following physical properties: mp 142–144 °C; ^1H NMR (CDCl_3) δ 0.93 (t, $J=7.5$ Hz, 6H), 1.28 (d, $J=5.5$ Hz, 6H), 1.54 (m, 4H), 3.64 (m, 2H), 3.90 (s, 3H), 5.86 (br s, 2H), 7.13 (s, 4H), and 8.07 (d, $J=15.5$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 161.3, 160.4, 131.0, 119.6, 116.5, 106.9, 57.8, 55.3, 29.6, 20.3, and 10.1; IR (neat) 1585 cm^{-1} ; HRMS (ES) m/z calcd for $\text{C}_{18}\text{H}_{29}\text{N}_2\text{O}$ 289.2274, found 289.2258.

4.1.9. *N*-(3-(2,4-Dimethoxybenzyl)amino)-2-(4-(methoxyphenyl)allylidene)-1-(2',4'-dimethoxyphenyl)methanaminium hexafluorophosphate (10i). This compound was prepared by the above procedure with the exception that 2,4-dimethoxybenzylamine was used in place of pyrrolidine in which case a 50% yield of a solid was obtained after flash chromatography. This material exhibited the following physical properties: mp 70–72 °C; ^1H NMR (CDCl_3) δ 3.76 (s, 6H), 3.82 (s, 6H), 3.86 (s, 3H), 4.53 (s, 4H), 6.44 (br s, 2H), 6.47 (dd, $J=2.0$, 8.5 Hz, 2H), 7.19 (d, $J=8.5$ Hz, 2H), 8.05 (br s, 2H); ^{13}C NMR (CDCl_3) δ 162.1, 161.6, 160.4, 158.5, 131.1, 130.8, 119.9, 116.1, 115.8, 106.7, 104.6, 98.7, 60.4, 55.4, 53.5, 49.7; IR (neat) 1584 cm^{-1} ; HRMS (ES) m/z calcd for $\text{C}_{28}\text{H}_{33}\text{N}_2\text{O}_5$ 477.2384, found 477.2341.

4.1.10. *N*-(3-(Butylamino)-2-(4-chlorophenyl)allylidene)butan-1-aminium hexafluorophosphate (10j). This compound was prepared by the above procedure with the exception that butylamine was used in place of pyrrolidine and the 4-chlorophenylvinamidinium salt was used in place of the 4-methoxyphenylvinamidinium salt in which case a 98% yield of a solid was obtained. This material exhibited the following physical properties: mp 156–158 °C; ^1H NMR (CDCl_3) δ 0.92 (t, $J=7.5$ Hz, 6H), 1.33 (m, 4H), 1.60 (m, 4H), 3.47 (br s, 4H), 6.42 (br s, 2H), 7.19 (d, $J=6.5$ Hz, 2H), 7.54 (d, $J=6.5$ Hz, 2H), and 7.81 (d, $J=14.5$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 162.5, 135.8, 131.3, 131.2, 126.3, 106.0, 49.9, 31.9, 19.4, and 13.4; IR (neat) 1602 cm^{-1} ; HRMS (ES) m/z calcd for $\text{C}_{17}\text{H}_{26}\text{ClN}_2$ 293.1779, found 293.1790.

4.1.11. *N*-(3-(Butylamino)-2-(3,4-dimethoxyphenyl)allylidene)butan-1-aminium hexafluorophosphate (10k). This compound was prepared by the above procedure with the exception that butylamine was used in place of pyrrolidine and the 3,4-dimethoxyphenylvinamidinium salt was used in place of the 4-methoxyphenylvinamidinium salt in which case a 97% yield of a solid was obtained. This material exhibited the following physical properties: mp 115–117 °C; ^1H NMR (CDCl_3) δ 0.94 (t, $J=7.2$ Hz, 6H), 1.34 (sextet, $J=7.2$ Hz, 4H), 1.60 (q, $J=7.2$ Hz, 4H), 3.50 (t, $J=7.2$ Hz, 4H), 3.90 (s, 3H), 3.94 (s, 3H), 6.68 (d, $J=1.8$ Hz, 1H), 6.76 (dd, $J=1.8$, 8.1 Hz, 1H), 7.05 (d, $J=8.1$ Hz, 1H), and 7.92 (b s, 2H); ^{13}C NMR (CDCl_3) δ 162.6, 150.5, 149.8, 122.6, 120.1, 113.2, 112.3, 107.2, 55.9, 55.8, 49.6, 31.9, 19.4, and 13.4; IR (neat) 1598 cm^{-1} ; HRMS (ES) m/z calcd for $\text{C}_{19}\text{H}_{31}\text{N}_2\text{O}_2$ 319.2380, found 319.2389.

4.1.12. *N*-(3-(Butylamino)-2-(*p*-tolyl)allylidene)butan-1-aminium hexafluorophosphate (10l). This compound was prepared by the above procedure with the exception that butylamine was used in place of pyrrolidine and the 4-methylphenylvinamidinium salt was

used in place of the 4-methoxy-phenylvinamidinium salt in which case a 97% yield of a solid was obtained. This material exhibited the following physical properties: mp 133–135 °C; ^1H NMR (CDCl_3) δ 0.93 (t, $J=7.5$ Hz, 6H), 1.33 (m, 4H), 1.57 (m, 4H), 2.43 (s, 3H), 3.47 (t, $J=7.5$ Hz, 4H), 7.10 (d, $J=8.1$ Hz, 2H), 7.39 (d, $J=8.1$ Hz, 2H), and 7.90 (s, 2H); ^{13}C NMR (CDCl_3) δ 162.5, 140.0, 131.7, 129.5, 124.7, 107.4, 49.6, 32.0, 21.2, 19.4, and 13.4; IR (neat) 1600 cm^{-1} ; HRMS (ES) m/z calcd for $\text{C}_{18}\text{H}_{29}\text{N}_2$ 273.2325, found 273.2334.

4.1.13. *N*-(3-(Butylamino)-2-(naphthalen-1-yl)allylidene)butan-1-aminium hexafluorophosphate (10m). This compound was prepared by the above procedure with the exception that butylamine was used in place of pyrrolidine and the 2-naphthylvinamidinium salt was used in place of the 4-methoxyphenylvinamidinium salt in which case a 97% yield of a solid was obtained. This material exhibited the following physical properties: mp 176–178 °C; ^1H NMR (CDCl_3) δ 0.87 (t, $J=7.5$ Hz, 6H), 1.25 (sextet, $J=7.5$ Hz, 4H), 1.50 (quintet, $J=7.5$ Hz, 4H), 3.42 (t, $J=7.5$ Hz, 4H), 7.43 (dd, $J=1.2$, 6.9 Hz, 1H), 7.58–7.69 (m, 4H), 7.98–8.01 (m, 2H), and 8.12 (br s, 2H); ^{13}C NMR (CDCl_3) δ 163.0, 134.6, 130.8, 130.5, 129.8, 129.3, 127.8, 127.2, 126.8, 124.7, 123.7, 104.9, 49.7, 31.9, 19.3, and 13.4; IR (neat) 1604 cm^{-1} ; HRMS (ES) m/z calcd for $\text{C}_{21}\text{H}_{29}\text{N}_2$ 309.2325, found 309.2440.

4.1.14. 1-(2-(4-Methoxyphenyl)allyl)pyrrolidine (11a). To a 100 mL round bottom flask equipped with a magnetic stir bar and condenser was added the amine exchanged vinamidinium salt (10a) (1.00 g, 2.64 mmol), sodium borohydride (0.300 g, 7.93 mmol), and 50 mL of anhydrous isopropanol. The resulting reaction mixture was refluxed for 24 h, allowed to cool to room temperature and was concentrated in vacuo. The crude residue was diluted with 100 mL of ethyl acetate and the organic layer was washed with water (3×50 mL) and brine (2×50 mL). The organic phase was dried over anhydrous Na_2SO_4 and was filtered and concentrated in vacuo to give a viscous oil. This material was subjected to flash chromatographic purification on a silica column using a Biotage SP-1 instrument and a hexane/ethyl acetate gradient in which case 0.510 g (89% yield) of an oil was obtained. This material exhibited the following physical properties: bp 148–150 °C at 1.6 Torr; ^1H NMR (CDCl_3) δ 1.78 (br s, 4H), 2.55 (br s, 4H), 3.46 (br s, 2H), 3.83 (s, 3H), 5.19 (s, 1H), 5.36 (s, 1H), 6.88 (d, $J=8.5$ Hz, 2H), and 7.49 (d, $J=8.5$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 159.0, 145.1, 133.1, 127.3, 113.6, 112.7, 61.0, 55.2, 54.2 and 23.6; HRMS (ES) m/z calcd for $\text{C}_{14}\text{H}_{20}\text{NO}$ 218.1539, found 218.1550.

4.1.15. 1-(2-(4-Methoxyphenyl)allyl)morpholine (11b)¹³. This compound was prepared according to the previous procedure with the exception that amine exchanged vinamidinium salt 10b was used. Chromatographic purification of the crude reaction product resulted in a 97% yield of a viscous oil, which exhibited the following physical properties: bp 85–86 °C at 0.19 Torr; ^1H NMR (CDCl_3) δ 2.50 (br s, 4H), 3.34 (br s, 2H), 3.71 (t, $J=5.0$ Hz, 4H), 3.84 (s, 3H), 5.18 (s, 1H), 5.44 (s, 1H), 6.88 (d, $J=9.0$ Hz, 2H), and 7.52 (d, $J=9.0$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 164.6, 148.5, 137.5, 132.6, 118.6, 118.3, 71.8, 68.6, 59.8, and 58.7; HRMS (ES) m/z calcd for $\text{C}_{14}\text{H}_{20}\text{NO}_2$ 234.1489, found 234.1498.

4.1.16. 1-(2-(4-Methoxyphenyl)allyl)piperidine (11c). This compound was prepared according to the previous procedure with the exception that amine exchanged vinamidinium salt 10c was used. Chromatographic purification of the crude reaction product resulted in a 97% yield of a viscous oil, which exhibited the following physical properties: bp 95–96 °C at 0.2 Torr; ^1H NMR (CDCl_3) δ 1.45 (m, 2H), 1.57 (m, 4H), 2.42 (broad absorption, 4H), 3.28 (s, 2H), 3.10 (s, 3H), 5.16 (s, 1H), 5.39 (s, 1H), 6.87 (d, $J=9.0$ Hz, 2H), and 7.51 (d, $J=9.0$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 159.1, 143.9, 133.3, 127.5, 113.5,

113.3, 64.0, 55.2, 54.6, 26.1, and 24.6; HRMS (ES) m/z calcd for $C_{15}H_{22}NO$ 232.1696, found 232.1717.

4.1.17. Diethyl-[2-(4-methoxyphenyl)-allyl]amine (11d). This compound was prepared according to the previous procedure with the exception that amine exchanged vinamidinium salt **10d** was used. Chromatographic purification of the crude reaction product resulted in a 96% yield of a viscous oil, which exhibited the following physical properties: bp 72–73 °C at 0.37 Torr; 1H NMR ($CDCl_3$) δ 1.04 (t, $J=7.0$ Hz, 6H), 2.57 (q, $J=7.0$ Hz, 4H), 3.42 (s, 2H), 3.83 (s, 3H), 5.22 (s, 1H), 5.38 (s, 1H), 6.88 (d, $J=6.5$ Hz, 2H), 7.49 (d, $J=6.5$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 159.1, 145.2, 133.2, 127.5, 113.5, 113.3, 57.9, 55.2, 46.8 and 11.5; HRMS (ES) m/z calcd for $C_{14}H_{22}NO$ 220.1696, found 220.1714.

4.1.18. Dipropyl-[2-(4-methoxyphenyl)-allyl]amine (11e). This compound was prepared according to the previous procedure with the exception that amine exchanged vinamidinium salt **10e** was used. Chromatographic purification of the crude reaction product resulted in a 99% yield of a viscous oil, which exhibited the following physical properties: bp 80–81 °C at 0.12 Torr; 1H NMR ($CDCl_3$) δ 0.87 (t, $J=7.5$ Hz, 6H), 1.5 (sextet, $J=7.5$ Hz, 4H), 2.43 (t, $J=7.5$ Hz, 4H), 3.42 (s, 2H), 3.85 (s, 3H), 5.24 (s, 1H), 5.39 (s, 1H), 6.89 (d, $J=8.5$ Hz, 2H), and 7.51 (d, $J=8.5$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 159.1, 145.5, 133.2, 127.6, 113.4, 113.1, 59.5, 55.9, 55.2, 20.1 and 11.9; HRMS (ES) m/z calcd for $C_{16}H_{26}NO$ 248.2009, found 248.1973.

4.1.19. *n*-Butyl-[2-(4-methoxyphenyl)-allyl]amine (11f). This compound was prepared according to the previous procedure with the exception that amine exchanged vinamidinium salt **10f** was used. Chromatographic purification of the crude reaction product resulted in a 62% yield of a solid, which exhibited the following physical properties: mp 140–145 °C; 1H NMR ($CDCl_3$) δ 0.89 (t, $J=7.5$ Hz, 3H), 1.28 (m, 2H), 1.63 (quintet, $J=7.5$ Hz, 2H), 2.98 (t, $J=7.5$ Hz, 2H), 3.85 (s, 3H), 4.20 (s, 2H), 5.47 (s, 1H), 5.64 (s, 1H), 6.98 (d, $J=8.4$ Hz, 2H), and 7.37 (d, $J=8.4$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 162.6, 160.5, 131.5, 119.5, 116.4, 107.1, 55.4, 49.6, 32.0, 19.4, and 13.4; IR (neat) 3258 cm^{-1} ; HRMS (ES) m/z calcd for $C_{14}H_{22}NO$ 220.1696, found 220.1714.

4.1.20. *n*-Hexyl-[2-(4-methoxyphenyl)-allyl]amine (11g). This compound was prepared according to the previous procedure with the exception that amine exchanged vinamidinium salt **10g** was used. Chromatographic purification of the crude reaction product resulted in a 99% yield of a viscous oil, which exhibited the following physical properties: bp 68–69 °C at 0.83 Torr; 1H NMR ($CDCl_3$) δ 0.87 (t, $J=6.9$ Hz, 3H), 1.25 (br s, 6H), 1.49 (m, 2H), 2.71 (t, $J=7.5$ Hz, 2H), 3.79 (s, 2H), 3.81 (s, 3H), 5.25 (s, 1H), 5.43 (s, 1H), 6.89 (d, $J=9.0$ Hz, 2H), and 7.35 (d, $J=9.0$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 159.8, 142.5, 130.7, 127.3, 114.8, 114.3, 55.3, 52.4, 48.4, 31.4, 28.2, 26.5, 24.4, and 13.9; IR (neat) 3200 cm^{-1} ; HRMS (ES) m/z calcd for $C_{16}H_{26}NO$ 248.2014, found 248.2080.

4.1.21. *s*-Butyl-[2-(4-methoxyphenyl)-allyl]amine (11h). This compound was prepared according to the previous procedure with the exception that amine exchanged vinamidinium salt **10h** was used. Chromatographic purification of the crude reaction product resulted in a 62% yield of a viscous oil, which exhibited the following physical properties: bp 78–79 °C at 0.23 Torr; 1H NMR ($CDCl_3$) δ 0.84 (t, $J=4.5$ Hz, 3H), 1.29 (d, $J=3.9$ Hz, 3H), 1.56 (m, 1H), 1.68 (m, 1H), 3.00 (m, 1H), 3.86 (s, 3H), 4.04 (d, $J=14.4$ Hz, 1H), 4.18 (d, $J=14.4$ Hz, 1H), 5.43 (s, 1H), 5.58 (s, 1H), 6.97 (d, $J=8.7$ Hz, 2H), and 7.38 (d, $J=8.7$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 160.4, 138.2, 128.4, 127.5, 119.2, 114.9, 56.0, 55.4, 49.0, 26.2, 15.7, and 9.4; IR (neat) 3227 cm^{-1} ; HRMS (ES) m/z calcd for $C_{14}H_{22}NO$ 220.1696, found 220.1730.

4.1.22. (2,4-Dimethoxybenzyl)-[2-(4-methoxyphenyl)-allyl]amine (11i). This compound was prepared according to the previous

procedure with the exception that amine exchanged vinamidinium salt **10i** was used. Chromatographic purification of the crude reaction product resulted in a 60% yield of a viscous oil, which exhibited the following physical properties: bp 128–129 °C at 0.81 Torr; 1H NMR ($CDCl_3$) δ 3.59 (s, 3H), 3.81 (s, 3H), 3.84 (s, 2H), 3.86 (s, 3H), 4.10 (s, 2H), 6.41 (d, $J=2.5$ Hz, 1H), 6.47 (dd, $J=2.5$, 8.0 Hz, 1H), 6.96 (d, $J=8.5$ Hz, 2H), 7.15 (d, $J=8.0$ Hz, 1H), and 7.32 (d, $J=8.0$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 162.4, 160.3, 158.6, 138.1, 132.2, 128.3, 127.4, 119.1, 114.6, 110.5, 105.1, 98.4, 60.5, 55.4, 55.2, 50.5, and 47.8; IR (neat) 3228 cm^{-1} ; HRMS (ES) m/z calcd for $C_{19}H_{24}NO_3$ 314.1751, found 314.1747.

4.1.23. *n*-Butyl-[2-(4-chlorophenyl)-allyl]amine (11j). This compound was prepared according to the previous procedure with the exception that amine exchanged vinamidinium salt **10j** was used. Chromatographic purification of the crude reaction product resulted in a 99% yield of a viscous oil, which exhibited the following physical properties: bp 72–73 °C at 0.25 Torr; 1H NMR ($CDCl_3$) δ 0.91 (t, $J=11.0$ Hz, 3H), 1.33 (m, 2H), 1.46 (sextet, $J=7.0$ Hz, 2H), 2.62 (t, $J=7.0$ Hz, 2H), 3.63 (s, 2H), 5.26 (s, 1H), 5.39 (s, 1H), 7.30 (d, $J=11.0$ Hz, 2H), and 7.38 (d, $J=11.0$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 145.2, 138.3, 133.4, 128.5, 127.5, 113.9, 53.3, 48.9, 31.9, 20.4, and 13.9; HRMS (ES) m/z calcd for $C_{13}H_{19}ClN$ 224.1201, found 224.1204.

4.1.24. *n*-Butyl-[2-(3,4-dimethoxyphenyl)-allyl]amine (11k). This compound was prepared according to the previous procedure with the exception that amine exchanged vinamidinium salt **10k** was used. Chromatographic purification of the crude reaction product resulted in a 99% yield of a viscous oil, which exhibited the following physical properties: bp 82–83 °C at 0.58 Torr; 1H NMR ($CDCl_3$) δ 0.87 (t, $J=7.2$ Hz, 3H), 1.28 (m, 2H), 1.47 (quintet, $J=7.2$ Hz, 2H), 2.67 (t, $J=7.2$ Hz, 2H), 3.70 (s, 2H), 3.86 (s, 3H), 3.88 (s, 3H), 5.21 (s, 1H), 5.37 (s, 1H), 6.82 (d, $J=9.0$ Hz, 1H), and 6.96 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 149.1, 149.0, 144.3, 132.0, 118.5, 113.7, 111.2, 109.6, 55.9, 53.0, 48.5, 31.1, 20.2, and 13.8; HRMS (ES) m/z calcd for $C_{15}H_{24}NO_2$ 250.1802, found 250.1807.

4.1.25. *n*-Butyl-[2-(4-methylphenyl)-allyl]amine (11l). This compound was prepared according to the previous procedure with the exception that amine exchanged vinamidinium salt **10l** was used. Chromatographic purification of the crude reaction product resulted in a 94% yield of a viscous oil, which exhibited the following physical properties: bp 82–83 °C at 0.48 Torr; 1H NMR ($CDCl_3$) δ 0.90 (t, $J=7.5$ Hz, 3H), 1.35 (sextet, $J=7.5$ Hz, 2H), 1.48 (quintet, $J=7.5$ Hz, 2H), 2.32 (s, 3H), 2.64 (t, $J=7.5$ Hz, 2H), 3.67 (s, 2H), 3.80 (s, 1H), 5.22 (s, 1H), 5.39 (s, 1H), 7.17 (d, $J=8.0$ Hz, 2H), 7.36 (d, $J=8.0$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 146.8, 137.4, 136.9, 128.8, 126.0, 111.3, 53.3, 48.7, 32.1, 20.2, and 13.4; IR (neat) 3262 cm^{-1} ; HRMS (ES) m/z calcd for $C_{14}H_{22}N$ 204.1747, found 204.1736.

4.1.26. *n*-Butyl-(2-naphthalen-1-yl-allyl)amine (11m). This compound was prepared according to the previous procedure with the exception that amine exchanged vinamidinium salt **10m** was used. Chromatographic purification of the crude reaction product resulted in a 98% yield of a viscous oil, which exhibited the following physical properties: bp 82–83 °C at 0.24 Torr; 1H NMR ($CDCl_3$) δ 0.90 (t, $J=7.2$ Hz, 3H), 1.34 (m, 2H), 1.46 (m, 2H), 2.71 (t, $J=7.2$ Hz, 2H), 3.69 (s, 2H), 5.27 (s, 1H), 5.62 (s, 1H), 7.33 (d, $J=6.9$ Hz, 1H), 7.44–7.52 (m, 3H), 7.81 (d, $J=8.1$ Hz, 1H), 7.86–7.89 (m, 1H), and 8.05 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 145.7, 139.1, 133.8, 131.4, 128.4, 127.7, 126.1, 125.4, 125.3, 116.7, 55.4, 48.7, 31.6, 20.4, and 13.9; HRMS (ES) m/z calcd for $C_{17}H_{22}N$ 240.1747, found 240.1789.

4.1.27. 1-Ethoxycarbonylmethyl-1-[2-(4-methoxyphenyl)-allyl]pyrrolidinium bromide (17a). To a round bottom flask equipped with

a magnetic stir bar was added allylic amine **11a** (0.250 g, 1.15 mmol), 10 mL of THF, and 0.992 g (1.15 mmol) of ethyl bromoacetate. The reaction mixture was stirred overnight at room temperature and the solvent was then removed in vacuo leaving 0.376 g (85% yield) of a light yellow solid, which exhibited the following physical properties: mp 134–136 °C; ^1H NMR (CDCl_3) δ 1.24 (t, $J=7.0$ Hz, 3H), 2.20 (m, 2H), 2.31 (m, 2H), 3.84 (s, 3H), 4.03 (m, 2H), 4.14 (q, $J=7.0$ Hz, 2H), 4.51 (s, 1H), 4.82 (s, 1H), 6.94 (d, $J=8.5$ Hz, 2H), and 7.37 (d, $J=8.5$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 165.1, 160.2, 137.9, 130.7, 127.9, 127.1, 114.6, 63.6, 62.6, 62.5, 58.3, 21.3, and 13.7; HRMS (ES) m/z calcd for $\text{C}_{18}\text{H}_{26}\text{NO}_3$ 304.1907, found 304.1964.

4.1.28. 4-(4-Methoxyphenyl)-2-pyrrolidin-1-yl-pent-4-enoic acid ethyl ester (18a). To a 100 mL round bottom flask equipped with a magnetic stir bar and condenser was added 0.029 g (1.18 mmol) of sodium hydride, and 30 mL of anhydrous acetonitrile. *tert*-Butanol (0.197 g 2.34 mmol) was added to the flask and the resulting mixture was allowed to react until gas evolution was no longer observed. Quaternary salt **17a** (0.351 g, 0.913 mmol) was added to the reaction mixture and the resulting solution was allowed to stir overnight. The reaction mixture was quenched with several mL of ethanol and the solvent was removed from the reaction mixture in vacuo. The resulting residue was dissolved in ethyl acetate (30 mL) and the ethyl acetate phase was then extracted with water (2 \times 30 mL) and brine (2 \times 30 mL) and dried over anhydrous sodium sulfate. After the ethyl acetate phase was filtered and concentrated in vacuo, the resulting residue was subjected to flash chromatographic purification on a silica column using a Biotage SP-1 instrument and a hexane/ethyl acetate gradient in which case 0.270 g (98% yield) of an oil was obtained. This material exhibited the following physical properties: bp 95–96 °C at 0.63 Torr; ^1H NMR (CDCl_3) δ 1.23 (t, $J=7.0$ Hz, 3H), 1.79 (br s, 4H), 2.63 (m, 2H), 2.80 (m, 2H), 2.93 (dd, $J=10.0$, 13.5 Hz, 1H), 3.00 (dd, $J=5.0$, 13.5 Hz, 1H), 3.30 (dd, $J=5.0$, 10.0 Hz, 1H), 3.83 (s, 3H), 4.09 (q, $J=7.0$ Hz, 2H), 5.06 (s, 1H), 5.27 (s, 1H), 6.87 (d, $J=7.0$ Hz, 2H), and 7.35 (d, $J=7.0$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 172.0, 159.2, 144.0, 132.9, 127.4, 113.9, 113.7, 65.7, 60.3, 55.3, 50.7, 37.7, 23.4, and 14.3; IR (neat) 1720 cm^{-1} ; HRMS (ES) m/z calcd for $\text{C}_{18}\text{H}_{26}\text{NO}_3$ 304.1907, found 304.1911.

4.1.29. 4-(4-Chlorophenyl)-2-dimethylaminopent-4-enoic acid ethyl ester (18b). Into a 50 mL round bottom flask equipped with a magnetic stir bar was placed 4.10 g (0.0210 mol) of 2-(4-chlorophenyl)-3-(*N,N*-dimethylamino)-1-propene¹ and 3.50 g (0.0210 mol) ethyl bromoacetate, and 25 mL of THF. The resulting mixture was stirred overnight at room temperature and the solvent was removed in vacuo leaving 8.13 g (100% yield) of a solid. Into a 250 mL 3-necked round bottom flask equipped with stir bar and condenser was placed 0.249 g (6.23 mmol) of a 60% dispersion of sodium hydride along with 50 mL of anhydrous acetonitrile. A 1.12 g sample (3.09 mmol) of the solid material from the previous step was dissolved in 50 mL of anhydrous acetonitrile and added to the reaction mixture. After stirring for 4 h at room temperature, the reaction mixture was concentrated in vacuo and the residue was partitioned between water (50 mL) and chloroform (50 mL) and the aqueous phase was extracted with additional chloroform (2 \times 50 mL). The combined organic phases were dried over anhydrous MgSO_4 , filtered and concentrated to yield a dark oil. The oil was purified by radial chromatography on a Harrison chromatotron using a 50:50 gradient of hexane/ethyl acetate in which case 1.05 g (90% yield) of an amber oil was obtained, which exhibited the following physical properties: bp 82–83 °C at 0.13 Torr; ^1H NMR (CDCl_3) δ 1.20 (t, $J=7.1$ Hz, 3H), 2.31 (s, 6H), 2.78 (dd, $J=5.8$, 14.0 Hz, 1H), 2.90 (dd, $J=9.0$, 14.0 Hz, 1H), 3.18 (dd, $J=5.8$, 9.0 Hz, 1H), 4.08 (q, $J=7.1$ Hz, 2H), 5.11 (s, 1H), 5.25 (s, 1H), and 7.28 (br s, 4H); ^{13}C NMR (CDCl_3) δ 171.9, 144.4, 139.5, 133.9, 129.0,

128.1, 116.0, 66.5, 60.4, 41.9, 36.2, and 14.6; IR (neat) 1726 cm^{-1} ; HRMS (ES) m/z calcd for $\text{C}_{15}\text{H}_{21}\text{ClNO}_2$ 282.1253, found 282.1255.

4.1.30. 4-(4-Methoxyphenyl)-2-dimethylaminopent-4-enoic acid ethyl ester (18c). This compound was prepared according to the previous procedure with the exception that 2-(4-methoxyphenyl)-3-(*N,N*-dimethylamino)-1-propene¹ was used as the allylic amine substrate. Chromatographic purification of the crude reaction product resulted in a 54% yield of a viscous oil, which exhibited the following physical properties: bp 89–90 °C at 0.13 Torr; ^1H NMR (CDCl_3) δ 1.19 (t, $J=7.1$ Hz, 3H), 2.32 (s, 6H), 2.79 (dd, $J=5.7$, 14.0 Hz, 1H), 2.90 (dd, $J=9.0$, 14.0 Hz, 1H), 3.22 (dd, $J=5.7$, 9.0 Hz, 1H), 3.78 (s, 3H), 4.07 (q, $J=7.1$ Hz, 2H), 5.01 (s, 1H), 5.20 (s, 1H), 6.83 (d, $J=8.9$ Hz, 2H), and 7.31 (d, $J=8.9$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 172.2, 159.8, 144.7, 133.4, 127.8, 114.2, 114.0, 66.8, 60.4, 55.6, 42.1, 36.3, and 14.6; IR (neat) 1726 cm^{-1} ; HRMS (ES) m/z calcd for $\text{C}_{16}\text{H}_{24}\text{NO}_3$ 278.1751, found 278.1734.

4.1.31. 4-(4-Bromophenyl)-2-dimethylaminopent-4-enoic acid ethyl ester (18d). This compound was prepared according to the previous procedure with the exception that 2-(4-bromophenyl)-3-(*N,N*-dimethylamino)-1-propene¹ was used as the allylic amine substrate. Chromatographic purification of the crude reaction product resulted in a 70% yield of a viscous oil, which exhibited the following physical properties: bp 98–99 °C at 0.40 Torr; ^1H NMR (CDCl_3) δ 1.20 (t, $J=7.1$ Hz, 3H), 2.31 (s, 6H), 2.78 (dd, $J=6.0$, 14.0 Hz, 1H), 2.90 (dd, $J=9.0$, 14.0 Hz, 1H), 3.18 (dd, $J=6.0$, 9.0 Hz, 1H), 4.08 (q, $J=7.1$ Hz, 2H), 5.12 (s, 1H), 5.27 (s, 1H), 7.23 (d, $J=8.6$ Hz, 2H), and 7.43 (d, $J=8.6$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 172.0, 144.5, 140.0, 132.0, 128.5, 122.0, 116.1, 66.5, 60.5, 42.0, 36.1, and 14.6; IR (neat) 1728 cm^{-1} ; HRMS (ES) m/z calcd for $\text{C}_{15}\text{H}_{21}\text{BrNO}_2$ 326.0750, found 326.0759.

4.1.32. 4-(Phenyl)-2-dimethylaminopent-4-enoic acid ethyl ester (18e). This compound was prepared according to the previous procedure with the exception that 2-(phenyl)-3-(*N,N*-dimethylamino)-1-propene¹ was used as the allylic amine substrate. Chromatographic purification of the crude reaction product resulted in a 67% yield of a viscous oil, which exhibited the following physical properties: bp 77–78 °C at 0.20 Torr; ^1H NMR (CDCl_3) δ 1.18 (t, $J=7.2$ Hz, 3H), 2.31 (s, 6H), 2.82 (dd, $J=5.8$, 14.0 Hz, 1H), 2.93 (dd, $J=9.0$, 14.0 Hz, 1H), 3.22 (dd, $J=5.8$, 9.0 Hz, 1H), 4.06 (q, $J=7.2$ Hz, 2H), 5.09 (s, 1H), 5.26 (s, 1H), and 7.22–7.39 (m, 5H); ^{13}C NMR (CDCl_3) δ 172.1, 145.5, 141.1, 128.9, 128.1, 126.8, 115.5, 66.7, 60.3, 42.0, 36.2, and 14.6; IR (neat) 1730 cm^{-1} ; HRMS (ES) m/z calcd for $\text{C}_{15}\text{H}_{22}\text{NO}_2$ 248.1645, found 248.1649.

4.1.33. 4-(3,4-Dimethoxyphenyl)-2-dimethylaminopent-4-enoic acid ethyl ester (18f). This compound was prepared according to the previous procedure with the exception that 2-(3,4-dimethoxyphenyl)-3-(*N,N*-dimethylamino)-1-propene¹ was used as the allylic amine substrate. Chromatographic purification of the crude reaction product resulted in a 62% yield of a viscous oil, which exhibited the following physical properties: bp 95–96 °C at 0.20 Torr; ^1H NMR (CDCl_3) δ 1.20 (t, $J=7.0$ Hz, 3H), 2.32 (s, 6H), 2.78 (dd, $J=5.9$, 14.0 Hz, 1H), 2.91 (dd, $J=9.0$, 14.0 Hz, 1H), 3.24 (dd, $J=5.9$, 9.0 Hz, 1H), 3.85 (s, 3H), 3.86 (s, 3H), 4.08 (q, $J=7.0$ Hz, 2H), 5.03 (s, 1H), 5.21 (s, 1H), 6.79 (d, $J=8.0$ Hz, 1H), 6.90 (s, 1H), and 6.92 (d, $J=8.0$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 172.2, 149.2, 145.0, 133.8, 119.0, 114.3, 111.2, 110.0, 66.8, 60.4, 56.2, 42.0, 36.3, and 14.7; IR (neat) 1734 cm^{-1} ; HRMS (ES) m/z calcd for $\text{C}_{17}\text{H}_{26}\text{NO}_4$ 308.1856, found 308.1861.

4.1.34. 4-(1-Naphthyl)-2-dimethylaminopent-4-enoic acid ethyl ester (18g). This compound was prepared according to the previous procedure with the exception that 2-(1-naphthyl)-3-(*N,N*-dimethylamino)-1-propene¹ was used as the allylic amine substrate. Chromatographic purification of the crude reaction product

resulted in a 72% yield of a viscous oil, which exhibited the following physical properties: bp 100–101 °C at 0.10 Torr; ^1H NMR (CDCl_3) δ 1.20 (t, $J=7.3$ Hz, 3H), 2.26 (s, 6H), 2.81 (dd, $J=5.5$, 14.0 Hz, 1H), 3.01 (dd, $J=9.0$, 14.0 Hz, 1H), 3.19 (dd, $J=5.5$, 9.0 Hz, 1H), 4.08 (q, $J=7.3$ Hz, 2H), 5.13 (s, 1H), 5.45 (s, 1H), 7.28 (m, 1H), 7.46 (m, 3H), 7.80 (m, 2H), and 8.02 (m, 1H); ^{13}C NMR (CDCl_3) δ 171.9, 145.5, 140.7, 134.3, 131.9, 128.8, 128.0, 126.4, 126.2, 125.9, 125.7, 118.5, 66.2, 60.4, 41.8, 38.9, and 14.7; IR (neat) 1728 cm^{-1} ; HRMS (ES) m/z calcd for $\text{C}_{19}\text{H}_{24}\text{NO}_2$ 298.1802, found 298.1795.

4.1.35. 4-(4-Methoxyphenyl)-2-piperidin-1-yl-pent-4-enoic acid ethyl ester (18h). This compound was prepared according to the previous procedure with the exception that 1-(2-(4-methoxyphenyl)-allyl) piperidine was used as the allylic amine substrate. Chromatographic purification of the crude reaction product resulted in a 40% yield of a viscous oil, which exhibited the following physical properties: bp 82–83 °C at 1.05 Torr; ^1H NMR (CDCl_3) δ 1.24 (t, $J=7.0$ Hz, 3H), 1.43 (m, 2H), 1.56 (m, 4H), 2.50 (br s, 2H), 2.63 (br s, 2H), 2.86 (m, 1H), 2.95 (m, 1H), 3.28 (m, 1H), 3.83 (s, 3H), 4.12 (q, $J=7.0$ Hz, 2H), 5.04 (s, 1H), 5.21 (s, 1H), 6.87 (d, $J=7.0$ Hz, 2H), and 7.34 (d, $J=7.0$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 171.6, 159.1, 144.7, 133.4, 127.4, 113.6, 113.4, 67.2, 59.8, 55.2, 53.4, 50.9, 35.8, 26.4, 24.6, and 14.7; IR (neat) 1709 cm^{-1} ; HRMS (ES) m/z calcd for $\text{C}_{19}\text{H}_{28}\text{NO}_3$ 318.2064, found 318.2057.

4.1.36. 4-(4-Methoxyphenyl)-2-dipropylaminopent-4-enoic acid ethyl ester (18i). This compound was prepared according to the previous procedure with the exception that dipropyl-[2-(4-methoxyphenyl)-allyl]amine was used as the allylic amine substrate. Chromatographic purification of the crude reaction product resulted in a 20% yield of a viscous oil, which exhibited the following physical properties: bp 81–82 °C at 0.93 Torr; ^1H NMR (CDCl_3) δ 0.85 (t, $J=7.5$ Hz, 6H), 1.25 (t, $J=7.5$ Hz, 3H), 1.35 (m, 4H), 2.43 (m, 2H), 2.57 (m, 2H), 2.75 (dd, $J=6.0$, 14.5 Hz, 1H), 3.00 (dd, $J=8.0$, 14.5 Hz, 1H), 3.45 (dd, $J=6.0$, 8.0 Hz, 1H), 4.12 (m, 2H), 5.04 (s, 1H), 5.24 (s, 1H), 6.88 (d, $J=9.0$ Hz, 2H) and 7.36 (d, $J=9.0$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 172.9, 159.1, 144.6, 133.1, 127.4, 113.6, 113.3, 62.0, 59.9, 55.3, 53.1, 36.3, 21.8, 14.5, and 11.7; IR (neat) 1729 cm^{-1} ; HRMS (ES) m/z calcd for $\text{C}_{20}\text{H}_{32}\text{NO}_3$ 334.2377, found 334.2356.

4.1.37. 1-(4-Bromophenyl)-2-dimethylamino-4-(4-methoxyphenyl)-pent-4-en-1-one (18j). Into a 50 mL round bottom flask equipped with a magnetic stir bar was placed 0.700 g (3.66 mmol) of 2-(4-methoxyphenyl)-3-(*N,N*-dimethylamino)-1-propene,¹ 0.994 g (3.58 mmol) of 2',4'-dibromo-2-bromoacetophenone, and 50 mL of THF. The resulting mixture was stirred for 2 h at room temperature and vacuum filtered to yield 1.65 g (98% yield) of a white solid, which was used without further purification. Into a 250 mL 3-necked round bottom flask equipped with stir bar and condenser was placed 0.086 g (3.60 mmol) of a 60% dispersion of sodium hydride along with 50 mL of anhydrous acetonitrile. A 1.30 g sample (2.77 mmol) of the solid material from the previous step was dissolved in 10 mL of anhydrous acetonitrile and added to the reaction mixture. After stirring for 2 h at room temperature, the reaction mixture was concentrated in vacuo and the residue was partitioned between water (50 mL) and chloroform (30 mL) and the aqueous phase was extracted with additional chloroform (2 \times 30 mL). The combined organic phases were dried over anhydrous MgSO_4 , filtered and concentrated to yield a dark oil. The oil was purified by radial chromatography on a Harrison chromatotron using a 50:50 gradient of hexane/ethyl acetate in which case 0.637 g (49% yield) of an amber oil was obtained, which exhibited the following physical properties: 130–131 °C at 1.20 Torr; ^1H NMR (CDCl_3) δ 2.31 (s, 6H), 2.88 (dd, $J=4.0$, 14.0 Hz, 1H), 3.04 (dd, $J=9.0$, 14.0 Hz, 1H), 3.80 (s, 3H), 4.10 (dd, $J=4.0$, 9.0 Hz, 1H), 4.94 (s, 1H), 5.11 (s, 1H), 6.82 (d, $J=9.0$ Hz, 2H), 7.24 (d, $J=9.0$ Hz, 2H), 7.48 (d, $J=8.7$ Hz, 2H), and 7.77 (d, $J=8.7$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 198.8,

159.8, 144.9, 136.7, 133.4, 132.2, 130.5, 128.5, 127.9, 114.6, 114.2, 65.9, 55.6, 41.8, and 31.4; IR (neat) 1686 cm^{-1} ; HRMS (ES) m/z calcd for $\text{C}_{20}\text{H}_{23}\text{BrNO}_2$ 388.0907, found 388.0891.

4.1.38. 2-Dimethylamino-4-(4-methoxyphenyl)-1-phenylpent-4-en-1-one (18k). This compound was prepared according to the previous procedure with the exception that 2-bromoacetophenone was used as the alkylating agent. Chromatographic purification of the crude reaction product resulted in a 76% yield of a viscous oil, which exhibited the following physical properties: 146–147 °C at 0.8 Torr; ^1H NMR (CDCl_3) δ 2.23 (s, 6H), 2.88 (dd, $J=4.0$, 13.9 Hz, 1H), 3.07 (dd, $J=9.5$, 13.9 Hz, 1H), 3.79 (s, 3H), 4.20 (dd, $J=4.0$, 9.5 Hz, 1H), 4.96 (s, 1H), 5.11 (s, 1H), 6.82 (d, $J=9.0$ Hz, 2H), 7.26 (d, $J=9.0$ Hz, 2H), 7.35 (t, $J=7.0$ Hz, 2H), 7.48 (t, $J=7.0$ Hz, 1H), and 7.78 (d, $J=7.0$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 199.8, 159.7, 145.0, 138.2, 133.6, 133.4, 129.0, 128.9, 127.9, 114.5, 114.2, 65.5, 55.6, 41.9, and 31.6; IR (neat) 1684 cm^{-1} ; HRMS (ES) m/z calcd for $\text{C}_{20}\text{H}_{24}\text{NO}_2$ 310.1802, found 310.1792.

4.1.39. 2-Dimethylamino-4-(4-methoxyphenyl)-1-(4-nitrophenyl)-pent-4-en-1-one (18l). This compound was prepared according to the previous procedure with the exception that 4'-nitro-2-bromoacetophenone was used as the alkylating agent. Chromatographic purification of the crude reaction product resulted in an 82% yield of a viscous oil, which exhibited the following physical properties: 128–129 °C at 0.4 Torr; ^1H NMR (CDCl_3) δ 2.32 (s, 6H), 2.90 (dd, $J=4.0$, 14.0 Hz, 1H), 3.07 (dd, $J=9.5$, 14.0 Hz, 1H), 3.79 (s, 3H), 4.10 (dd, $J=4.0$, 9.5 Hz, 1H), 4.96 (s, 1H), 5.14 (s, 1H), 6.84 (d, $J=8.8$ Hz, 2H), 7.25 (d, $J=8.8$ Hz, 2H), 7.95 (d, $J=9.0$ Hz, 2H), and 8.19 (d, $J=9.0$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 197.8, 159.8, 150.5, 144.8, 142.5, 133.2, 130.0, 127.8, 124.1, 114.8, 114.3, 67.1, 55.8, 42.0, and 30.7; IR (neat) 1694 cm^{-1} ; HRMS (ES) m/z calcd for $\text{C}_{20}\text{H}_{23}\text{N}_2\text{O}_4$ 355.1652, found 355.1541.

4.1.40. [3-(4-Methoxyphenyl)-1-(2-nitrophenyl)-but-3-enyl]dimethylamine (18m). This compound was prepared according to the previous procedure with the exception that 2-nitrobenzyl bromide was used as the alkylating agent. Chromatographic purification of the crude reaction product resulted in a 21% yield of a viscous oil, which exhibited the following physical properties: 129–130 °C at 0.9 Torr; ^1H NMR (CDCl_3) δ 2.21 (s, 6H), 2.76 (dd, $J=10.0$, 14.0 Hz, 1H), 3.21 (dd, $J=4.8$, 14.0 Hz, 1H), 3.79 (s, 3H), 4.14 (dd, $J=4.8$, 10.0 Hz, 1H), 4.74 (s, 1H), 5.07 (s, 1H), 6.79 (d, $J=9.0$ Hz, 2H), 7.18 (d, $J=9.0$ Hz, 2H), 7.27 (t, $J=7.0$ Hz, 1H), 7.42 (t, $J=7.0$ Hz, 1H), 7.50 (d, $J=8.0$ Hz, 1H), and 7.56 (d, $J=8.0$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 159.7, 151.9, 144.9, 136.1, 133.7, 132.0, 129.9, 128.1, 127.7, 124.2, 114.4, 114.1, 62.4, 55.6, 42.9, and 37.7; IR (neat) 1527 and 1360 cm^{-1} ; HRMS (ES) m/z calcd for $\text{C}_{19}\text{H}_{23}\text{N}_2\text{O}_3$ 327.1703, found 327.1711.

4.1.41. [3-(4-Methoxyphenyl)-1-(4-nitrophenyl)-but-3-enyl]dimethylamine (18n). This compound was prepared according to the previous procedure with the exception that 4-nitrobenzyl chloride was used as the alkylating agent. Chromatographic purification of the crude reaction product resulted in an 53% yield of a viscous oil, which exhibited the following physical properties: 128–129 °C at 0.9 Torr; ^1H NMR (CDCl_3) δ 2.19 (s, 6H), 2.68 (dd, $J=11.4$, 14.7 Hz, 1H), 3.33 (m, 2H), 3.81 (s, 3H), 4.63 (s, 1H), 4.94 (s, 1H), 6.82 (d, $J=8.0$ Hz, 2H), 7.13 (d, $J=8.0$ Hz, 2H), 7.20 (d, $J=8.0$ Hz, 2H), and 8.08 (d, $J=8.0$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 159.8, 149.0, 147.6, 144.9, 133.4, 129.8, 128.0, 123.6, 114.9, 114.2, 69.2, 55.6, 43.4, and 40.1; IR (neat) 1513 and 1346 cm^{-1} ; HRMS (ES) m/z calcd for $\text{C}_{19}\text{H}_{23}\text{N}_2\text{O}_3$ 327.1703, found 327.1722.

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Supplementary data

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