Synthesis and Reactivity of *N*-Substituted-1-amino-2-(methylsulfonyl)-3-phenyl-2-propenes[1]

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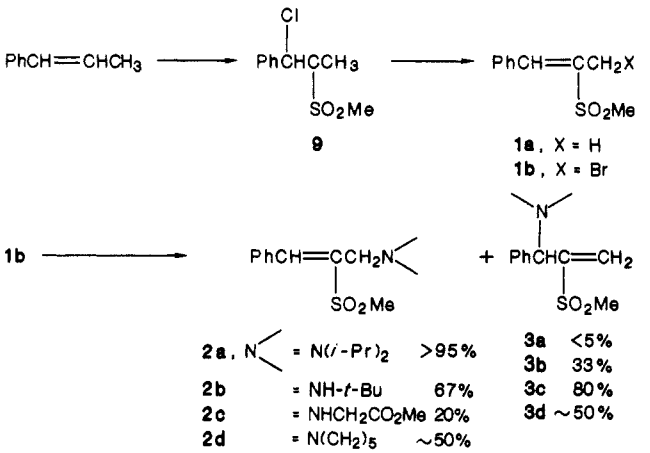
The synthesis of 3-bromo-2-(methylsulfonyl)-1-phenyl-1-propene (**1b**) is described. Reaction of the allyl bromide **1b** with *tert*-butylamine, diisopropylamine, glycine methyl ester, and piperidine in benzene solution yielded mixtures of direct substitution (S_N2) and substitution-rearrangement (S_N2') products, **2** and **3**, respectively. The S_N2:S_N2' ratio ranged from 1:4 for reaction of **1b** with glycine methyl ester to greater than 20:1 for the reaction with diisopropylamine. Amine hydrochloride promoted amine exchange reactions of *N*,*N*-diisopropyl-1-amino-2-(methylsulfonyl)-3-phenyl-2-propene (**2a**) and the amine exchange and aminotropic rearrangement reactions of the thermodynamically less stable *N*-*tert*-butyl-1-amino-2-(methylsulfonyl)-1-phenyl-2-propene (**3b**) are described. Evidence for acid-catalyzed aminotropic rearrangement and amine exchange reactions (**3** → **2**) is presented. Equilibrium constants for reactions of **2a** and of **2b** with piperidine hydrochloride in chloroform solution were determined.

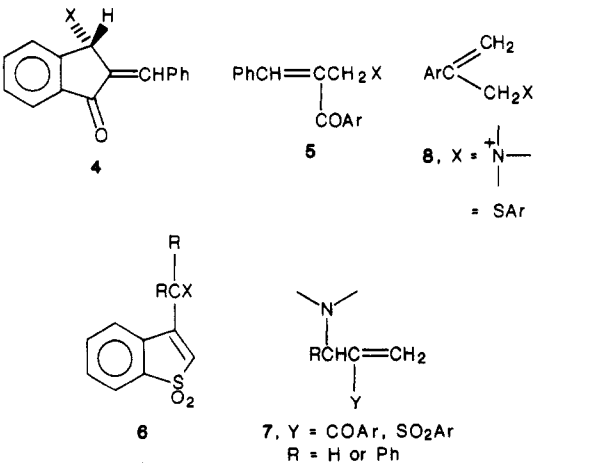
Introduction

Several reports have appeared in the literature regarding substitution-rearrangement reactions of negatively substituted allyl substrates (e.g., **4**, **5**, and **6**) in nonpolar solvents.[2-4] Evidence for a bimolecular substitution-rearrangement (S_N2') mechanism was presented for reactions of 2-aroylallyl halides (**4** and **5**) with alkylamines in hydrocarbon solvents. By analogy, the 2-(methylsulfonyl)allyl bromide **1b** would be expected to react via a bimolecular substitution-rearrangement (S_N2') mechanism in benzene solution. Previous investigations demonstrated that [2-(arylsulfonyl)allyl]- and [2-aroylallyl]amines **7** underwent facile amine exchange reactions with simple *N*-alkylamines in nonpolar solvents.[4,5] More recently, we showed that simple [2-aroylallyl]amines (**7**, R = H, Y = COAr) react readily (in dilute chloroform or methanol solution at room temperature) with *N*-alkylamine hydrohalides to yield amine exchange products.[6] In the previous paper, we showed that aminotropic rearrangements in [2-(phenylsulfonyl)allyl]amino substrates are catalyzed by *N*-alkylamine hydrochlorides and that the rate of rearrangement is solvent dependent.[7]

Lawton and co-workers reported a comprehensive investigation of several activated aryl-substituted allyl substrates **8** that served as cross-linking reagents for proteins by equilibrium transfer alkylation.[8] In this report, product studies for reactions of [2-(methylsulfonyl)allyl]amines (**2** and **3**) with nucleophilic reagents are described. Substitution reactions and equilibrium alkylations of [2-(methylsulfonyl)allyl]amines (**2** and **3**) with amine hydrohalides were examined as models for reactions of activated allyl substrates with ammonium groups in peptides, proteins, and nucleic acids.

Scheme I





Results and Discussion

The parent system, 2-(methylsulfonyl)-1-phenylpropene (**1a**), was synthesized in 86% overall yield by the copper(II)-catalyzed addition of methanesulfonyl chloride to 1-phenylpropene followed by dehydrochlorination of the adduct (**9**) with *N*-methylpiperidine in benzene.[9] Reaction of 2-(methylsulfonyl)-1-phenylpropene (**1a**) with *N*-

(1) Presented in part at the 187th National Meeting of the American Chemical Society, St. Louis, MO, April 10-13, 1984; ORGN 107.
(2) George, A. D.; Doomes, E.; Cromwell, N. H. *J. Org. Chem.* **1971**, *36*, 3918.
(3) Maury, G.; Wu, E.-M.; Cromwell, N. H. *J. Org. Chem.* **1968**, *33*, 1900.
(4) Doomes, E.; Thiel, P. A.; Nelson, M. L. *J. Org. Chem.* **1976**, *41*, 248.
(5) Cromwell, N. H.; Matsumoto, K.; George, A. D. *J. Org. Chem.* **1971**, *36*, 272. Maury, G.; Cromwell, N. H. *J. Org. Chem.* **1969**, *34*, 596.
(6) Doomes, E.; Sadeghi, A. G.; Carter, R. Abstracts of the 37th Southwest Regional American Chemical Society Meeting, San Antonio, TX, December 9-11, 1981, Paper No. 123. Doomes, E.; Sadeghi, A. G.; Gardner, J. D.; Dillon, B. S.; Green, C. S.; Cromwell, N. H., unpublished results.
(7) Doomes, E.; Clarke, U. R.; Neitzel, J. J. *J. Org. Chem.*, preceding paper in this issue.
(8) Mitra, S.; Lawton, R. G. *J. Am. Chem. Soc.* **1979**, *101*, 3097.
(9) Goralski, C. T.; Truce, W. E. *J. Org. Chem.* **1970**, *35*, 4220.

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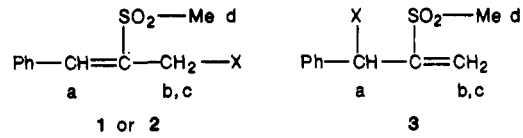
Table I. Physical Data for 1-3



compd	^{1}H NMR spectral data[a] H_a	H_b, H_c	H_d	R^b	mass spectra M^+ (% base peak)
1a, X = H	7.66	2.28	2.96		
1b, X = Br	7.78	4.50	3.18		274, 276 (2.8, 2.4)
1c, X = OCH_3	7.80	4.36	3.02	3.42	226 (8.7), 147 (26)
2a, X = N(*i*-Pr)$_2$	7.84	3.69	3.18	0.85, 2.88	298 (2.2), 280 (45)
2b, X = NH-*t*-Bu	7.66	3.65	3.07	1.10, 1.30	267 (0.6), 252 (88)
3b, X = NH-*t*-Bu	4.90	6.30	2.40	1.07, 1.35	
2c, X = $NHCH_2CO_2CH_3$	7.73	3.80	3.12	2.17, 3.45, 3.65	283 (0.4), 224 (24)
3c, X = $NHCH_2CO_2CH_3$	4.83	6.61, 6.16	2.53	2.20, 3.33, 3.69	
2d, X = N$(CH_2)_5$	7.84	3.54	3.24	1.44, 2.32	279 (4.7), 199 (71)
3d, X = N$(CH_2)_5$	4.35	6.46, 6.37	2.47	1.44, 2.32	

[a] Chemical Shifts are reported in δ units. H_a, H_b, H_c, and H_d are singlets. [b] Expected multiplicities and relative intensities were observed for the N-alkyl substituents. The phenyl group gave the expected signal also.

bromosuccinimide in the presence of a catalytic amount of benzoyl peroxide in refluxing carbon tetrachloride solution gave a 47% yield of the yellow crystalline allyl bromide **1b**. The bromine atom was introduced with relative ease (greater than 95% conversion of **1a** to **1b** was achieved within 24 h) compared to bromination of the analogous 2-(arylsulfonyl)allyl system.[4,7] The 2-(methylsulfonyl)allyl bromide (**1b**) reacted with diisopropylamine, *tert*-butylamine, glycine methyl ester, and piperidine to yield mixtures of direct substitution (S_N2) and substitution rearrangement (S_N2') products, **2** and **3**, respectively (Scheme I). A bimolecular mechanism (S_N2 or S_N2') is probable for the reaction of **1b** with *N*-alkylamines in the nonpolar aprotic solvent. The methanolysis reaction of **1b** is relatively slow, indicating that carbocationic reactions are inhibited by the 2-methylsulfonyl group.[10,11] Additionally, the bulkier *N*-alkylamines gave the higher direct substitution/substitution rearrangement product ratios. Since **3c** and **3d** rearrange readily to **2c** and **2d**, respectively, the observed product distributions in these cases do not reflect kinetic product ratios.[12] However, we showed that the *N*-*tert*-butylamino substrate **3b** is stable under the reaction conditions. The reaction of propenyl bromide **1b** (0.21 M) with diisopropylamine (1.0 M) in benzene solution was sluggish (3 days required for completion) compared to its reactions with less bulky amines. The S_N2':S_N2 ratio was the same regardless to the percent conversion of **1b** to diisopropylamino substrates (**2a** and **3a**).[13] In contrast, the reaction of **1b** (0.036 M) with piperidine (0.084 M) in benzene solution was approximately 63% complete in only 5 min, and the proportion of **2d** increased with an increase in reaction time (and percent conversion).

The *N*,*N*-diisopropyl[2-(methylsulfonyl)allyl]amino substrate **2a** reacted with piperidine hydrochloride in refluxing chloroform solution to yield the (1-piperidinyl)allyl substrate **2d** in greater than 95% conversion. Also, the *N*-*tert*-butyl[2-(methylsulfonyl)allyl]amino system **2b** reacted readily with piperidine hydrochloride and glycine methyl ester hydrochloride in chloroform under the same conditions to give **2d** and **2c** in ~87% and ~73% yields, respectively. However, the *N*,*N*-diisopropylallylamino substrate **2a** did not react with *tert*-butylamine hydrochloride upon prolonged heating in chloroform solution. These data indicate that the reactivity of the substituted [2-(methylsulfonyl)allyl]amino substrate is sensitive to the steric requirement of the *N*-alkyl group in the attacking nucleophile. Under the reaction conditions, these amine hydrochloride catalyzed amine exchange reactions are reversible. The equilibrium constant (k_{eq} = 12) for the 1-piperidinyl/*N*,*N*-diisopropylamino (**2d**/**2a**) exchange reaction indicates that the *N*,*N*-diisopropylamino substrate (**2a**) is thermodynamically less stable than the (1-piperidinyl)allyl system (**2d**) by approximately 1.8 kcal/mol (that may be attributed to steric compression in **2a** at 61 °C). However, the equilibrium constant for the 1-piperidinyl/*N*-*tert*-butylamino exchange reaction is relatively small, k_{eq} = 1.6. Equilibrium constants for these reactions were determined readily by utilizing ^{1}H NMR spectrometry, focusing on intensities of signals for methyl groups and allyl protons (see the Experimental Section for calculations, and Table I). Although equilibration between glycine methyl ester hydrochloride and *N*-*tert*-butylallylamino substrate **2b** (and *N*,*N*-diisopropylallylamino substrate **2a**) occurred, we did not attempt to calculate equilibrium constants for these reactions since portions of the hydrochloride remained suspended. Equilibrium constants for reactions of **2a** and of **2b** with piperidine hydrochloride suggest that exchange should occur between *N*,*N*-diisopropylamino substrate **2a** and *tert*-butylamine hydrochloride with a reasonably large equilibrium constant, $k_{eq} \simeq 7.5$. Interestingly, this amine exchange reaction does not occur upon prolonged treatment of **2a** with either excess *tert*-butylamine hydrochloride or a mixture of *tert*-butylamine and its hydrochloride in refluxing chloroform.

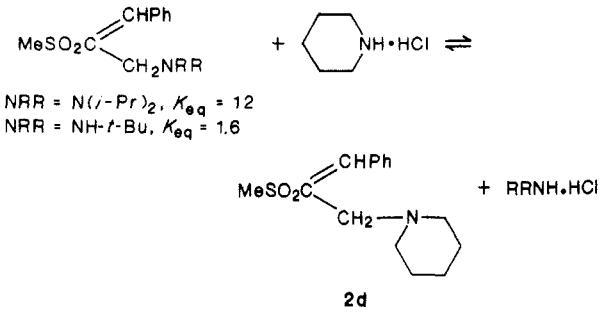
The *N*-*tert*-butyl[2-(methylsulfonyl)allyl]amino system **3b** rearranged readily to the thermodynamically more stable isomer **2b** when treated with either *tert*-butylamine or *tert*-butylamine hydrochloride in refluxing chloroform solution. On the other hand, a purified sample of **3b** was recovered unchanged after refluxing in chloroform for 24 h. Additionally, this allylamino compound (**3b**) was stable

(10) The apparent rate of methanolysis of **1b** is less than half the apparent rate for 3-bromo-1-phenylpropene. See the Experimental Section for details.

(11) Ammonium salts of simple allyl amines are stable under the reaction conditions: Young, W. G.; Webb, I. D.; Goering, H. L. *J. Am. Chem. Soc.* **1951**, *73*, 1036.

(12) The suggestion by a referee that the product ratios could be determined in the presence of excess amine and amine hydrohalide is not feasible since we have shown that amine hydrohalide and excess amine promote rearrangement in these activated allylamino substrates.[4,7]

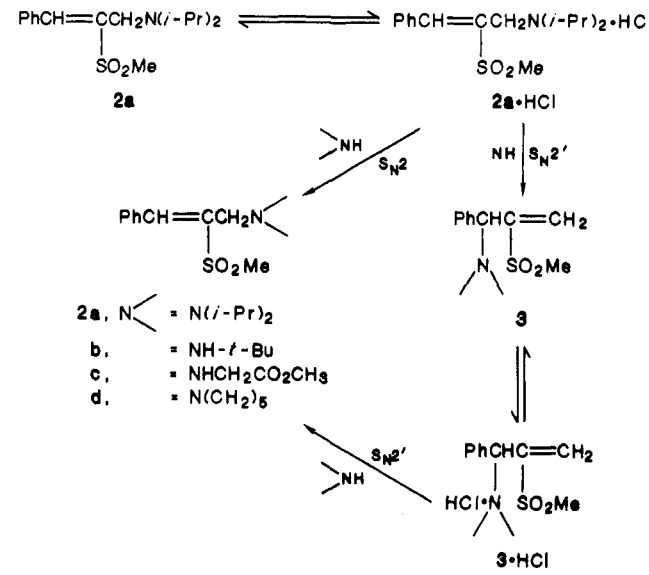
(13) *N*,*N*-Diisopropyl-1-amino-1-phenyl-2-(phenylsulfonyl)-2-propene, an analogue of **2a**, was stable toward rearrangement in refluxing chloroform that contained diisopropylamine hydrobromide.[7] Also, previous reports indicate that β-keto allylamino substrates do not react with excess diisopropylamine to yield rearranged product.[3,5]



in chloroform solution that contained either *tert*-butylamine or *tert*-butylamine hydrochloride for 24 h at room temperature. For comparison, the analogous [2-(arylsulfonyl)allyl]amino system (7, Y = SO_2Ar, R = Ph) rearranged readily under the latter reaction conditions.[4] These data indicate that the energy barrier for the rearrangement reaction of the *N-tert*-butyl[2-(methylsulfonyl)allyl]amino system (**3b** → **2b**) is relatively high, and the ease of rearrangement is sensitive to the nature of the *electron-withdrawing group at position-2*. Analogous amine exchange reactions occur when *N-tert*-butyl-1-amino-2-(methylsulfonyl)-1-phenyl-2-propene (**3b**) is treated with either glycine methyl ester hydrochloride or piperidine hydrochloride to yield **2c** or **2d**, respectively. The exchange occurred between **3b** and the amine hydrochloride in the presence of the thermodynamically more stable isomer (**2b**), indicating the higher reactivity of the former compound (see Experimental Section).

The possible mechanistic routes for the amine hydrochloride promoted amine exchange reactions (**2b** → **2c** or **2d**, and **3b** → **2c** and **2d**) and for the aminotropic rearrangement (**3b** → **2b**) are summarized in Scheme II. The equilibrium established between the added *N*-alkylamine hydrochloride and the substrate (**2** or **3**) converts a fraction of the amino moiety in the latter into a good leaving group (e.g., **2a**·HCl or **3**·HCl). Thus a reasonable mechanism for conversion of **3b** to **2b** is an S_N2'-type reaction on the hydrochloride of **3b** by *tert*-butylamine (**3b** → **3b**·HCl → **2b**, Scheme II). Similarly, S_N2'-type reactions are probable for conversion of **3b** to **2c** and to **2d**. Conversion of **2a** to **2d** would require two consecutive S_N2'-type reactions on intermediate hydrochlorides of **2a** and **3d**. Alternately, direct substitution (S_N2) on **2a**·HCl by free amine may occur (Scheme II). The glycine methyl ester hydrochloride and piperidine hydrochloride promoted amine exchange reactions can be rationalized in terms of analogous acid–base equilibria (**3** → **3**·HCl) followed by S_N2'-type reactions (**3**·HCl → **2**). Since direct substitution (S_N2) and substitution–rearrangement (S_N2') products (**2** and **3**) are observed for reactions of propenyl bromide **1b** under kinetically controlled conditions, it is probable that these mechanisms compete also in the amine exchange reactions of **2a** and **2b**. However, the bulkiness of the *N,N*-diisopropylamino group in **2a** and the fact that it is a poor leaving group compared to bromide would favor an S_N2' reaction for the amine exchange reaction of this substrate (**2a**).[14] Experimental[15] and theoretical[16] evidence indicate that the preferred stereochemistry for the S_N2' reaction is a syn relationship between an amine nucleophile and the leaving group at the transition state. The inertness

Scheme II



of the *N,N*-diisopropylallylamino substrate **2a** toward *tert*-butylamine hydrochloride may be due to the inaccessibility of a syn relationship between the attacking bulky *tert*-butylamine and the departing bulky diisopropylamine in the transition state for the S_N2' reaction.

Experimental Section

General Procedures. All melting points were obtained with a Mel-Temp melting point apparatus and are uncorrected. Infrared spectra were recorded on a Beckman Microlab 600MX spectrophotometer. The 60-MHz ^1H NMR spectra were determined on a Varian EM-360A NMR spectrometer with tetramethylsilane as an internal standard and are reported in δ units. Low-resolution (70 eV) mass spectra were obtained on a Hewlett Packard 5985 GC/MS spectrometer. Elemental analyses were obtained from MicAnal Organic Microanalysis, Tuscon, AZ. A summary of ^1H NMR and mass spectral data is presented in Table I. The composition of mixtures of products was determined by comparing intensities of appropriate ^1H NMR signals (Table I), and crude reaction products were analyzed by this method in each case.

2-(Methylsulfonyl)-1-phenyl-1-propene (1a). A mixture of 11.8 g (0.10 mol) of 1-phenylpropene, 11.5 g (0.10 mol) of methanesulfonyl chloride, 0.13 g (1.0 mmol) of anhydrous cupric chloride, 0.21 g (1.5 mmol) of *N*-methylpiperidine hydrochloride, and 4.0 g of acetonitrile were heated at 100 °C for 2 h while it was stirred magnetically. The cooled reaction mixture was a dark brown semisolid that consisted of 1-chloro-2-(methylsulfonyl)-1-phenylpropene (**9**) primarily (based on the ^1H NMR spectrum of the crude material and comparison with the spectrum of a purified sample of **9**, see below). The reaction product (**9**) was dissolved in 50 mL of benzene, and a 10.2-g (0.10 mol) sample of *N*-methylpiperidine was added. The mixture was heated at reflux for 3 h, cooled to room temperature, and gravity-filtered. The filtrate was washed with 30 mL of 5% hydrochloric acid and with two 30-mL portions of water. The benzene was separated and removed under reduced pressure. A 17.3-g (88% yield) sample of yellow oil (**1a**) was obtained. The ^1H NMR spectrum was consistent with the assigned structure.

The solid that was obtained (prior to dehydrochlorination) was recrystallized from methanol to yield pale yellow crystals of 1-chloro-1-phenyl-2-(methylsulfonyl)propane (**9**), mp 107–108 °C. Anal. Calcd for $C_{10}H_{13}SO_2Cl$: C, 51.61; H, 5.63; Cl, 15.23. Found: C, 51.70; H, 5.75; Cl, 15.17.

3-Bromo-2-(methylsulfonyl)-1-phenyl-1-propene (1b). A 17.1-g (0.087 mol) sample of **1a** and 17.0 g (0.096 mol) of *N*-bromosuccinimide were added to 50 mL of carbon tetrachloride and the mixture was heated to a gentle reflux. A solution of 0.30 g of benzoyl peroxide in 25 mL of carbon tetrachloride was added dropwise to the refluxing mixture over a 2 h period. Refluxing

(14) Substitution–rearrangement products were observed directly for reactions of an analogous 2-(arylsulfonyl)allylamino substrate with *N*-alkylamine hydrochlorides.[7]

(15) Stork, G.; Kreft, A. F., III *J. Am. Chem. Soc.* **1977**, *99*, 3850, 3851. Magid, R. M.; Fruchery, O. S. *J. Am. Chem. Soc.* **1979**, *101*, 2107.

(16) Yates, R. L.; Epiotis, N. D.; Bernardi, F. *J. Am. Chem. Soc.* **1975**, *97*, 6615. Liotta, C. L. *Tetrahedron Lett.* **1975**, 523.

was continued for 24 h and the reaction mixture was filtered while hot to remove suspended solids. Evaporation of the solvent under reduced pressure yielded a yellow solid. The product was decolorized with charcoal and recrystallized from methanol to yield 13.0 g (54%) of fluffy white crystals of **1b**, mp 110–111 °C. Anal. Calcd for $C_{10}H_{11}SO_2Br$: C, 43.65; H, 4.03; Br, 29.04. Found: C, 43.49; H, 3.98; Br, 28.93.

***N,N*-Diisopropyl-1-amino-2-(methylsulfonyl)-3-phenyl-2-propene (2a).** A 2.0-g (0.0073 mol) sample of propenyl bromide **1b** and 3.6 g (0.036 mol) of diisopropylamine were dissolved in 35 mL of benzene, the mixture was allowed to react at room temperature for 4 days while it was stirred magnetically. The reaction mixture was washed with two 20-mL portions of water. The benzene layer was separated, dried (K_2CO_3), and evaporated under reduced pressure. A quantitive yield of a yellow oil was obtained that crystallized upon standing. Analysis of the crude reaction product by ^1H NMR spectrometry indicated that at least 95% of the material was **2a**. Recrystallization of the product from methanol yielded 1.50 g (70%) of pale yellow crystals of **2a**, mp 75–76 °C. Anal. Calcd for $C_{16}H_{25}NO_2S$: C, 65.05; H, 8.53; N, 4.74. Found: C, 64.92; H, 8.71; N, 4.63.

***N*-*tert*-Butyl-1-amino-2-(methylsulfonyl)-3-phenyl-2-propene (2b) and *N*-*tert*-Butyl-1-amino-2-(methylsulfonyl)-1-phenyl-2-propene (3b).** A 1.0-g (0.0036 mol) sample of propenyl bromide **1b** and 0.80 g (0.011 mol) of *tert*-butylamine were dissolved in 15 mL of benzene and allowed to react at room temperature for 24 h. The reaction mixture was diluted with an additional 15 mL of benzene and washed with two 20-mL portions of water. The benzene layer was dried over anhydrous potassium carbonate and evaporated under reduced pressure. A quantitative yield of a pale yellow oil was obtained. The ^1H NMR spectrum of the oil indicated that **2b** and **3b** were present in a 2:1 ratio.

The mixture of **2b** and **3b** was dissolved in 6 mL of chloroform, 0.20 g (0.0018 mol) of *tert*-butylamine hydrochloride was added, and the mixture was heated at reflux for 6 h. The chloroform solution was diluted with 25 mL of the same solvent and was washed with two 20-mL portions of water. The chloroform layer was dried (anhydrous K_2CO_3) and evaporated to yield a yellow oil whose ^1H NMR spectrum indicated the presence of **2b** only. The product (**2b**) was crystallized from an ether–hexane mixture (0.64 g, 66%), mp 56–57 °C. Anal. Calcd for $C_{14}H_{21}NO_2S$: C, 62.89; H, 7.92; N, 5.24. Found: C, 62.60; H, 8.11; N, 5.05.

1-(Methyl *N*-glycinyl)-2-(methylsulfonyl)-3-phenyl-2-propene (2c). A 0.50-g (0.0018 mol) sample of propenyl bromide **1b**, 0.45 g (0.0036 mol) of glycine methyl ester hydrochloride, and 0.40 g (0.0040 mol) of *N*-methylpiperidine were added to 15 mL of chloroform. The mixture was heated at reflux temperature for 24 h. The reaction mixture was diluted with 15 mL of chloroform and washed with two 15-mL portions of water and dried (K_2CO_3) and the chloroform was removed under reduced pressure to yield 0.46 g (90%) of a light brown oil. The ^1H NMR spectrum of the oil indicated the presence of **2c** as the major component (90%) and **3c** as a minor product. Since we showed that the kinetically favored product (**3c**) reacts with glycine methyl ester hydrochloride in chloroform to yield predominantly the thermodynamically more stable isomer **2c**, this is the probable path by which **2c** is formed in this experiment rather than strictly a solvent or temperature effect on the product distribution. The tan oil was crystallized from an ether–hexane mixture to yield 0.36 g (70%) of yellow crystals of **2c**, mp 89–90 °C. Anal. Calcd for $C_{13}H_{17}NO_4S$: C, 55.11; H, 6.05; N, 4.94. Found: C, 54.95; H, 5.70; N, 4.88.

1-(Methyl *N*-glycinyl)-2-(methylsulfonyl)-1-phenyl-2-propene (3c). A 0.50-g (0.0018 mol) sample of propenyl bromide **1b**, 0.45 g (0.0036 mol) of glycine methyl ester hydrochloride, and 0.40 g (0.0040 mol) of *N*-methylpiperidine were added to 15 mL of benzene. The reagents were mixed throughly and the reaction was allowed to proceed for 24 h. The reaction mixture was diluted with 15 mL of benzene, washed with two 20-mL portions of water, and dried (Na_2SO_4), and the solvent was evaporated under reduced pressure. A pale yellow oil (0.48 g, 93%) was obtained that crystallized upon standing. ^1H NMR spectral analysis indicated that the reaction mixture consisted of **3c** and **2c** in a 4:1 ratio. Recrystallization of the solid from methanol yielded 0.34 g (67%) of **3c**, mp 70–71 °C. Anal. Calcd for $C_{13}H_{17}NO_4S$: C, 55.11; H, 6.05; N, 4.94. Found: C, 55.08; H, 6.01; N, 4.91.

1-(1-Piperidinyl)-2-(methylsulfonyl)-3-phenyl-2-propene (2d) and 1-(1-Piperidinyl)-2-(methylsulfonyl)-1-phenyl-2-propene (3d). Propenyl bromide **1b** (0.50 g, 0.0018 mol) and 0.36 g (0.0042 mol) of piperidine were dissolved in 50 mL of benzene and allowed to react for 5 min while the solution was stirred magnetically. The benzene solution was washed twice with 50-mL portions of water. The benzene layer was separated, dried ($MgSO_4$), and evaporated under reduced pressure. The residue was dissolved in deuteriochloroform and the ^1H NMR spectrum was determined immediately. The ^1H NMR spectra of purified samples of **1b** and **2d** were utilized to analyze the spectrum of the crude mixture. The spectrum of the crude mixture indicated that propenyl bromide **1b** remained (~37%) and that allylamino products **2d** and **3d** (~63% overall) were present in a 50:50 ratio. When the reaction was repeated and the reaction time increased to 30 min, only ~9% of the propenyl bromide remained, and the ratio of **2d** to **3d** was 4:1. When the reaction was allowed to proceed for 3 h, ^1H NMR analysis of the crude product indicated the presence of allylamino substrate **2d** only. The usual workup yielded 0.32 g (63%) of white crystalline **3d** from ether–hexane, mp 58–59 °C.

1-(1-Piperidinyl)-2-(methylsulfonyl)-3-phenyl-2-propene (2d). A 0.40-g (0.0014 mol) sample of *N,N*-diisopropylallylamine **2a** and 0.80 g (0.0066 mol) of piperidine hydrochloride were dissolved in 10 mL of chloroform and allowed to react at reflux temperature for 4 days. The chloroform solution was washed with two 15-mL portions of water. The chloroform solution was dried ($MgSO_4$) and evaporated under reduced pressure to yield 0.36 g (95%) of a yellow oil that crystallized upon standing. The ^1H NMR spectrum of the reaction product indicated the presence of **2d** (~98%) and **2a** (~2%). Compound **2d** was obtained as a white crystalline solid from an ether–hexane mixture, mp 58–59 °C. When a 0.40-g (0.0014 mol) sample of **2a** and 0.40 g (0.0033 mol) of piperidine hydrochloride were dissolved in 10 mL of chloroform and allowed to react at reflux temperature for 4 days, 21% of **2a** remained. These data were used to calculate an equilibrium constant for this reaction. Anal. Calcd for $C_{15}H_{21}NO_2S$: C, 64.48; H, 7.58; N, 5.01. Found: C, 64.40; H, 7.83; N, 4.96.

Reaction of 2b with *N*-Alkylamine Hydrochlorides. A 0.40-g (0.0015 mol) sample of *N*-*tert*-butylaminopropene **2b** and 0.0070 mol of *N*-alkylamine hydrochloride were dissolved in 20 mL of chloroform. The mixture was heated at reflux temperature for 4 days. The solution was diluted with 15 mL of chloroform, washed with two 20-mL portions of water, dried ($MgSO_4$), and evaporated under reduced pressure. The residue was analyzed by ^1H NMR spectrometry. Reaction of glycine methyl ester hydrochloride with **2b** led to ~73% conversion to **2c**, while reaction of **2b** with piperidine hydrochloride led to ~87% conversion to **2d**. When 0.50 g (0.0019 mol) of **2b** and 0.50 g (0.0041 mol) of piperidine hydrochloride (in 20 mL of chloroform) were heated at reflux for 3 days, a 75% conversion of **2b** to **2d** was observed. Equilibrium constants for the interconversions of **2b** to **2d** were calculated on the basis of ^1H NMR spectral analysis of the reaction mixtures (see Table I). Although equilibration of **2b** and **2c** occurred, we did not attempt to calculate an equilibrium constant since a portion of the glycine methyl ester hydrochloride remained suspended in the chloroform solution.

Calculation of Equilibrium Constants. The general approach for calculating equilibrium constants is illustrated with the interconversion of **2b** and **2d**. $[\mathbf{2b}]_i$ and $[\mathbf{2b}]_e$ equal initial

$$\mathbf{2b} + B \rightleftarrows \mathbf{2d} + C$$

$$k_{eq} = \frac{[\mathbf{2d}]_e[C]_e}{[\mathbf{2b}]_e[B]_e}$$

and equilibrium concentrations of **2b**, respectively. $[B]_i$ and $[B]_e$ equal initial and equilibrium concentrations of attacking amine hydrochloride, respectively. $[\mathbf{2d}]_i$ and $[\mathbf{2d}]_e$ equal initial and equilibrium concentrations of **2d**, respectively. $[C]_i$ and $[C]_e$ equal initial and equilibrium concentrations of released amine hydrochloride.

The percent conversion of **2b** to **2d** was determined by comparing intensities of signals for protons in the methylsulfonyl groups, and cross-checking by comparing intensities of signals for protons in the *N*-alkyl groups in the ^1H NMR spectra of

mixtures (see Table I). The percents of components used to calculate equilibrium constants are average values from two or three trials at a given concentration. When 0.50 g (0.00187 mol) of **2b** and 0.50 g (0.00411 mol) of piperidine hydrochloride in 20 mL of chloroform were heated at reflux for 3 days, a 75% conversion of **2b** to **2d** was observed. The stoichiometry of the reaction requires the following relationships.

$$[\mathbf{2d}]_e = [C]_e = (\%\ \text{convn of } \mathbf{2b} \text{ to } \mathbf{2d}) \times [\mathbf{2b}]_i$$

$$[\mathbf{2b}]_e = [\mathbf{2b}]_i - (\%\ \text{convn of } \mathbf{2b} \text{ to } \mathbf{2d}) \times [\mathbf{2b}]_i$$

$$[B]_e = [B]_i - (\%\ \text{convn of } \mathbf{2b} \text{ to } \mathbf{2d}) \times [\mathbf{2b}]_i$$

Therefore

$$[\mathbf{2d}]_e = [C]_e = 0.75 \times \frac{0.00187\ \text{mol}}{0.020\ \text{L}} = 0.0701$$

$$[\mathbf{2b}]_e = \frac{0.00187\ \text{mol}}{0.020\ \text{L}} - 0.0701 = 0.0234$$

$$[B]_e = \frac{0.00411\ \text{mol}}{0.020\ \text{L}} - \left[0.75 \times \frac{0.00187\ \text{mol}}{0.20\ \text{L}}\right] =$$

$$0.2055 - 0.0701 = 0.1354$$

$$k_{eq} = \frac{[\mathbf{2d}]_e[C]_e}{[\mathbf{2b}]_e[B]_e} = \frac{0.701 \times 0.701}{0.0234 \times 0.1354}$$

$$k_{eq} = 1.6$$

Attempted Reaction of *N,N*-Diisopropylaminopropene 2a with *tert*-Butylamine Hydrochloride and *tert*-Butylamine. A 0.50-g (0.0017 mol) sample of diisopropylaminopropene **2a**, 0.40 g (0.0037 mol) of *tert*-butylamine hydrochloride, and 0.20 g (0.0027 mol) of *tert*-butylamine were dissolved in 10 mL of chloroform and heated at reflux temperature for 3 days. The solution was diluted with 25 mL of chloroform and washed with two 20-mL portions of water. Evaporation of the solvent led to the recovery of 0.46 g (92%) of **2a** only (based on the ^{1}H NMR spectrum). The *tert*-butylamino products (**2b** and **3b**) could not be detected by ^{1}H NMR spectrometry.

Attempted Reaction of 2a with *tert*-Butylamine Hydrochloride. *N,N*-Diisopropylallylamino substrate **2a** (0.50 g, 0.0017 mol) and 1.0 g (0.0093 mol) of *tert*-butylamine hydrochloride (a portion remained suspended) were added to 20 mL of chloroform. The mixture was heated at reflux temperature for 6 days while it was stirred. The solution was diluted with 20 mL of chloroform, washed with two 25-mL portions of water, dried ($MgSO_4$), and evaporated under reduced pressure. This led to a quantitative recovery (0.48 g, 96%) of a yellow oil that crystallized upon cooling. ^{1}H NMR spectral analysis of this solid indicated that **2a** was the only detectable product.

Reaction of 2a with Glycine Methyl Ester Hydrochloride. A 0.20-g (0.00071 mol) sample of diisopropylaminopropene **2a** and 0.20 g (0.0016 mol) of glycine methyl ester hydrochloride were dissolved in 15 mL of chloroform. The reaction mixture was heated at reflux for 24 h, diluted with 15 mL of chloroform, and washed with two 10-mL portions of water. The chloroform was evaporated under reduced pressure to yield a yellow oil that consisted of **2a** only, based on ^{1}H NMR spectral analysis. Treatment of 0.20 g (0.00071 mol) of diisopropylaminopropene **2a** with 0.25 g (0.0020 mol) of glycine methyl ester hydrochloride in 20 mL of refluxing chloroform for 4 days led to a 25% conversion of **2a** to **2c** (^{1}H NMR analysis).

Attempted Reaction of *N,N*-Diisopropylaminopropene 2a with *N*-Methylpiperidine Hydrochloride/Methanol. A 0.40-g (0.0014 mol) sample of **2a** and 0.80 g (0.0059 mol) of *N*-methylpiperidine hydrochloride were dissolved in 6 mL of methanol, and the mixture was heated at reflux temperature for 24 h. The methanol was evaporated under reduced pressure, and the mixture was dissolved in 20 mL of dichloromethane, washed with two 15 mL portions of water, and dried ($MgSO_4$). Evaporation of the dichloromethane led to recovery of 0.36 g (90%) of the reactant **2a** (no other product could be detected by ^{1}H NMR analysis of the crude mixture).

2-(Methylsulfonyl)-3-methoxy-1-phenylpropene (1c). A 0.50-g (0.0018 mol) sample of **1b** was dissolved in 20 mL of anhydrous methanol, and the solution was heated at reflux temperature for 4 h. Evaporation of the solvent followed by ^{1}H NMR analysis indicated that the reaction mixture consisted of the methanolysis product **1c** (34%) and the starting propenyl bromide **1b** (64%).

Methanolysis of 3-Bromo-1-phenyl-1-propene (10a). A 0.50-g (0.0025 mol) sample of **10a** was dissolved in 20 mL of anhydrous methanol, and the solution was heated at reflux temperature for 4 h. Evaporation of the methanol followed by ^{1}H NMR analysis of the mixture indicated a 75% conversion of propenyl bromide **10a** to 3-methoxy-1-phenyl-1-propene (**10b**).

Reaction of 2a with Piperidine. A 0.40-g (0.0014 mol) sample of diisopropylaminopropene **2a** and 0.60 g (0.0071 mol) of piperidine were dissolved in 10 mL of chloroform and heated at reflux for 3 days. The solution was diluted with 15 mL of chloroform, washed with two 25-mL portions of water, dried ($MgSO_4$), and evaporated under reduced pressure. The ^{1}H NMR spectrum of the crude product indicated a 33% conversion of **2a** to the piperidino compound **2d**.

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