Use of Hine's *D* Values To Predict the Position of the Equilibrium in the Cope Rearrangement of Multiply Substituted 1,5-Dienes

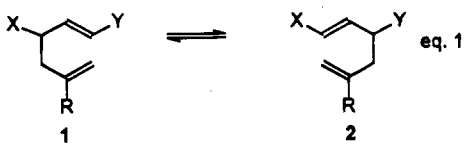
James P. Hagen,* Kemberly D. Lewis, Scott W. Lovell, Paolo Rossi, and Ayse Z. Tezcan

Department of Chemistry, University of Nebraska at Omaha, Omaha, Nebraska 68182-0109

Received May 30, 1995[⊗]

A series of 1,5-dienes (**1a-f**) were employed to test whether Hine's *D* values can predict the position of equilibrium in Cope rearrangements. In the cases of the substituent pairs [OCH_3, H], [OCH_3, CH_3], [$N(CH_3)_2$, H], [$N(CH_3)_2$, CH_3], and [$N(CH_3)_2$, OCH_3], equilibrium constants calculated with Hine's *D* values gave reasonable agreement with those obtained experimentally. Dienes **1g-i** were prepared to test whether reduction of the π-donating character of a nitrogen substituent (carbamoyl vs dimethylamino) would change the directing ability of the nitrogen group. The aggregate order of directing ability was $N(CH_3)_2$ > OCH_3 > $EtO_2CN(CH_3)$ > CH_3 > H. Diene **15a**, with a more complicated substitution pattern (OCH_3 and CH_3 versus CH_3 and H) not directly amenable to analysis with *D* values, can be considered to reduce to the case of [OCH_3, H]. The experimental K_{eq} obtained agreed with that expected for the [OCH_3, H] pair. Dienes **15c** and **16b**, designed to test the pairs [CH_3, SPh] and [OCH_3, SPh], respectively, decomposed under the gas phase conditions of the rearrangement. Attempts to effect rearrangement with Pd(II) catalysis failed.

The effect of various combinations of substituents on the rate and position of equilibrium in the Cope rearrangement has often been reported.[1] In particular, many reports have involved systems where X is an anionic oxygen (eq 1). This group leads to large accelerations in rate and strongly favors the right side of the equilibrium.



eq. 1

1 **2**

a) X = OCH_3, Y = H, R = H

b) X = OCH_3, Y = CH_3, R = H

c) X = OCH_3, Y = CH_3, R = CH_3

d) X = $N(CH_3)_2$, Y = H, R = H

e) X = $N(CH_3)_2$, Y = CH_3, R = H

f) X = $N(CH_3)_2$, Y = OCH_3, R = H

g) X = $N(CH_3)(CO_2Et)$, Y = H, R = H

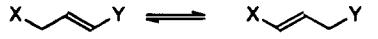
h) X = $N(CH_3)(CO_2Et)$, Y = CH_3, R = H

i) X = $N(CH_3)(CO_2Et)$, Y = OCH_3, R = H

j) X = SCH_3, Y = H, R = H

Little attention has been paid to cooperative equilibrium effects between multiple noncharged substituents in simple acyclic cases. Kirmse investigated the effect of single heteroatom substituents on the activation parameters of the rearrangement using compounds **1a**, **d**, and **j**.[2] He observed complete Cope rearrangement with **1a** and **d**, whereas **j** rearranges only in part. He concluded that variation of substituents has a minor effect on reaction rate but a major effect on the equilibrium constant and invoked heteroatom stabilization of the double bond to explain the equilibrium effects.

Hine has developed a table of double bond stabilizing abilities (*D* values) of diverse groups which permits prediction of free energy changes in allylic isomerizations (eq 2).[3] A Cope rearrangement is analogous to this



eq. 2

isomerization in that an allyl group rather than a hydrogen atom is migrating. Substitution of the allyl group for the hydrogen atom should not greatly perturb the thermodynamics of the system. Thus, one can hypothesize that Hine's table of *D* values may serve as a qualitative and perhaps semiquantitative guide to equilibrium constants in the Cope rearrangement when multiple substituents are involved.

The first goal of this study was to apply the postulated predictive value of Hine's *D* values in a systematic way to Cope systems. Consequently, an array of such substrates was synthesized. Secondly, since the *D* value of a group parallels its π-donating ability, we hypothesized that modification of a group's π-donating ability might reverse the inherent directing ability. Thus, while **1d, e**, and **f** should rearrange to **2d, e**, and **f** with a rather large K_{eq}, carbamate **1i** should have a rather small K_{eq} due to the comparatively lower π-donating character of carbamoyl versus dimethylamino.

Results

Syntheses of Substrates. Oxygen-containing dienes **1b** and **c** were made conventionally by Grignard addition to the appropriate aldehyde followed by methylation (eq

⊗ Abstract published in *Advance ACS Abstracts,* October 15, 1995.

(1) For example: (a) Curran, D. P.; Suh, Y.-G. *J. Am. Chem. Soc.* **1984**, *106*, 5002. (b) Rozeboom, M. D.; Kiplinger, J. P.; Bartmess, J. E. *J. Am. Chem. Soc.* **1984**, *106*, 1025. (c) Burrows, C. J.; Carpenter, B. K. *J. Am. Chem. Soc.* **1981**, *103*, 6984. (d) Miyashi, T.; Hazato, A.; Mukai, T. *J. Am. Chem. Soc.* **1980**, *104*, 891. (e) Jang, M. E.; Hudspeth, J. P. *J. Am. Chem. Soc.* **1980**, *102*, 2463. (f) Evans, D. A.; Steigerwald, M. L.; Goddard, W. A. *J. Am. Chem. Soc.* **1979**, *101*, 1994. (g) Ireland, R. C.; Mueller, R. H.; Willard, A. K. *J. Am. Chem. Soc.* **1976**, *98*, 2868.

(2) Dollinger, M.; Henning, W.; Kirmse, W. *Chem. Ber.* **1982**, *115*, 2309.

(3) Hine, J.; Skoglund, M. J. *J. Org. Chem.* **1982**, *47*, 4766.

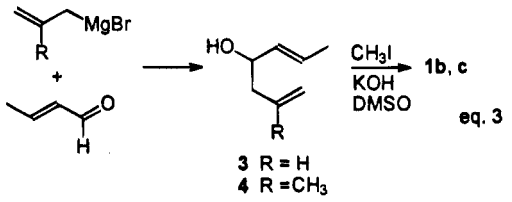
0022-3263/95/1960-7471$09.00/0 © 1995 American Chemical Society

Table 1. Comparison of Calculated K_{eq} vs Experimental K_{eq}

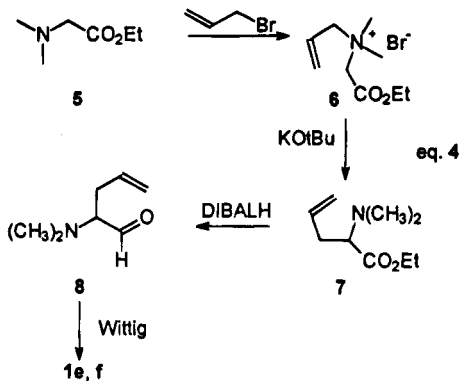
1	X	Y	R	ΔG_{XY}	T °C	K_{eq}calcd	K_{eq}exp
a	OCH_3	H	H	−4.87[a] (−4.93)[b] [−4.99][c]	240	119 (126) [134]	>50[d]
b	OCH_3	CH_3	H	−1.96 (−1.46) [−0.765]	320	5.27 (3.45) [1.92]	1.5
c	OCH_3	CH_3	CH_3	−1.96 (−1.46) [-0.826]	290	5.76 (3.69) [2.09]	1.4
d	$N(CH_3)_2$	H	H	−6.83 (−7.46) [−8.13]	240	811 (1504) [2905]	>50[d]
e	$N(CH_3)_2$	CH_3	H	−3.92 (−4.65) [−5.54]	280	35.4 (68.7) [155]	>50
f	$N(CH_3)_2$	OCH_3	H	−1.96 (−2.53) [−3.23]	280	5.94 (9.99) [18.9]	10[e]
g	carbamoyl	H	H	NA	290	NA	23.2, 23.5
h	carbamoyl	CH_3	H	NA	290	NA	16[f]
i	carbamoyl	OCH_3	H	NA	290	NA	<0.02[g]

[a] The calculations were done according to Hine and Skoglund.[3] The direction of reaction is *trans*-$XCH_2CH{=}CHY \rightarrow$ *trans*-$XCH{=}CHCH_2Y$, where $\Delta G_{XY} = D_Y - D_X$. [b] The values in parentheses are the K_{eq} calculated using Hine's corrected ΔG values which allow for polar interactions across the *trans*-vinylene group. The equation is $\Delta G_{XY} = D_Y - D_X + \tau_v(\sigma_X\sigma_{CH_2Y} - \sigma_Y\sigma_{CH_2X})$, where "the σ constants are Hammett para substituent constants and τ_v is a proportionality constant that was treated as a disposable parameter."[3] [c] The bracketed values were corrected as described in the text. [d] Kirmse[2] reports kinetic data on these systems using a number of temperatures. At no temperature did he report detecting residual starting material. Therefore, an equilibrium constant of at least 50 was assumed. [e] This value was estimated from the rearrangement of the *Z* isomer; the *E* isomer was apparently much less reactive. [f] Reaction time = 80 min. [g] No rearrangement to **2i** was detected by NMR; only *Z* to *E* isomerization was observed.

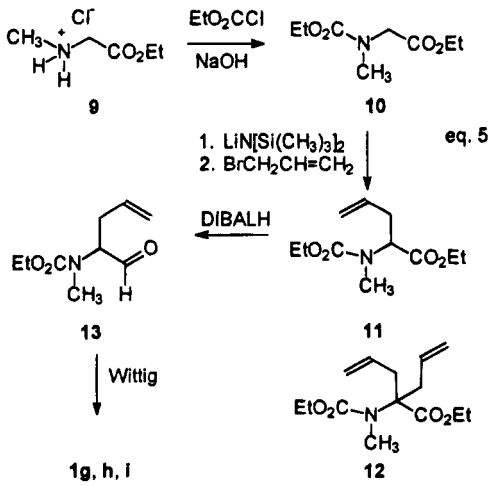
3). The amino-substituted dienes **1e** and **f** were made



from **5** via allylation, [2,3] sigmatropic rearrangement, reduction, and Wittig olefination (eq 4). Carbamates **1g-i**



were derived from **9** via ethoxycarbonylation, allylation, reduction, and olefination (eq 5).



Cope Rearrangements. Compounds **1** rearranged to **2** at a convenient rate in the gas phase at 290 °C. The ratio of **2** to **1** was determined by NMR. In Table 1, the resulting K_{eq} values are compared to those calculated using Hine's *D* values.

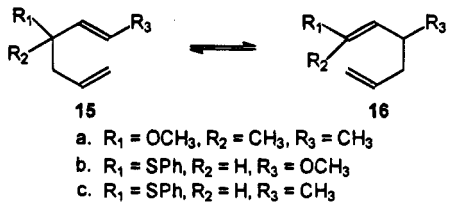
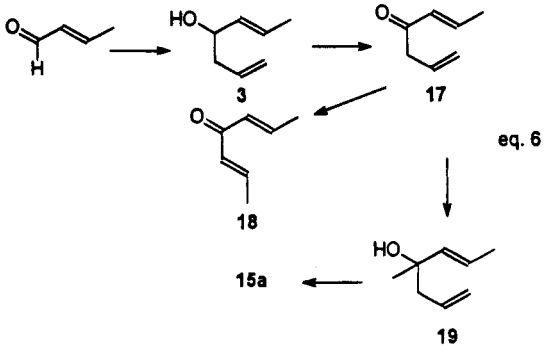


Figure 1.

Other substrates were made that did not have a simple substitution pattern directly amenable to analysis with *D* values (**15a**) or that decomposed under the rearrangement conditions (**15c** and **16b**). Figure 1 summarizes these.

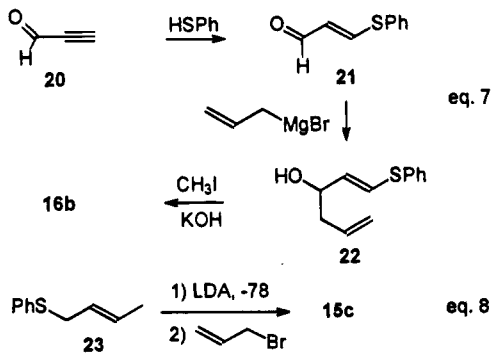
The synthesis of **15a** (eq 6) was complicated by isomerization of **17** to the conjugated isomer **18**.[4-6] Not only



were varying amounts of undesired isomers present in the **17/18** product mixture depending on the oxidation method used, but once separated, **17** rearranged to **18** even at −20 °C.[7-11]

(4) Gibson, T.; Erman, W. *J. Org. Chem.* **1972**, *37*, (8), 1159.
(5) Snowden, R. L.; Linder, S. M.; Muller, B. L.; Schulte-Elte, K. H. *Helv. Chim. Acta* **1987**, *70*, 1858.
(6) Majetich, G.; Casares, A.; Chapman, D.; Behnke, M. *J. Org. Chem.* **1986**, *51*, 1745.
(7) Four oxidation methods were tried. PCC oxidation caused considerable rearrangement to 1,4-heptadien-6-one.[8] The method of Attenburrow, employing MnO_2, consumed starting material but gave no **17**.[9] We postulate cleavage to intermediate radicals which give volatile side products. Swern oxidation was reasonably successful with a cold and rapid workup to minimize **15** formation.[10] The most successful oxidation in terms of the least amount of rearrangement was the chromium trioxide/pyridine method of Ratcliff and Rodehorst.[11]
(8) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, *16*, 2647.
(9) Attenburrow, J.; Cameron, A.; Chapman, J.; Evans, R.; Hems, B.; Jansen, A.; Walker, T. *J. Chem. Soc.* **1952**, 1094.

The synthesis of **16b** from propynal was accomplished as indicated in eq 7. LDA promoted allylation of **23** gave **15c** (eq 8).



Cope Rearrangements. Multiply substituted **15a** rearranged to a mixture of *E*/*Z* **16a**. Hydrolysis of **16a** produced almost exclusively 4-methylhept-6-en-2-one (**24**), indicating nearly complete rearrangement. Sulfides **15c** and **16b** decomposed in the gas phase.

Discussion

The equilibrium between **1** and **2** should be determined by the substituent *D* values in the order $N(CH_3)_2 > OCH_3 > CH_3 > H$. This expectation was confirmed by the results (Table 1). Note that the order of the experimental K_{eq} values follows that predicted by calculation. Also observe that the values calculated with corrections for *trans*-vinylene interactions show closer agreement than those calculated without this correction. The table further shows that the β-methallyl group (**1c**) gives a K_{eq} comparable to that found with the allyl group as expected.

Why do the experimental K_{eq} values not agree more closely with Hine's values as corrected for *trans*-vinylene interactions? Hine's τ_v parameter was introduced to correct for *trans*-vinylene interactions as shown in eq 9,

$$\Delta G_{XY} = D_Y - D_X + \tau_v(\sigma_X\sigma_{CH_2Y} - \sigma_\gamma\sigma_{CH_2X}) \quad (9)$$

where "the σ constants are Hammett para substituent constants and τ_v is a proportionality constant that was treated as a disposable parameter."[3] One would expect a significant alteration in the τ_v value due to the gas phase conditions of the rearrangement. Hine suggests a "10−20% increase in this value on going from the liquid to the gas phase."[12] Any increase in τ_v would yield more positive ΔG values, giving smaller calculated K_{eq} values more closely in agreement with experiment. In addition, Hine's τ_v parameter was applied to a series of reactions done preferentially at 25 °C or extrapolated to that temperature. The parameter τ_v depends linearly on temperature as shown in eq 10 where "ρ is the reaction

$$\tau_v = 2.3RT\rho^2/[\log K_1 - \log(4K_2)] \quad (10)$$

constant for *trans* 3-substituted acrylic acids and K_1 and K_2 are the first and second ionization constants of fumaric acid."[12] Since our reactions were conducted at 290 °C or higher, ΔG should be additionally positive and the K_{eq} values further lowered, giving closer agreement with experiment.

Using eq 9 and Hine's values for ΔG_{XY} before and after correction, a new value can be calculated for the second term. The data for **1c**, along with Hine's value of τ_v = 10.6,[3] generate eq 11. This gives 0.0472 for ($\sigma_X\sigma_{CH_2Y}$ -

$$1.96 - 1.46 = 10.6(\sigma_X\sigma_{CH_2Y} - \sigma_Y\sigma_{CH_2X}) \quad (11)$$

$\sigma_Y\sigma_{CH_2X}$).[13] Assuming a 20% increase in τ_v due to the gas phase conditions, the 10.6 value becomes 12.72. Some temperature adjustment is needed for τ_v as indicated by eq 10. Thus, solving eq 10 for the constant term using *T*

$$\tau_v = 12.72 = 2.3RT\rho^2/[\log K_1 - \log(4K_2)] = (\text{constant})T \quad (12)$$

= 298.15 K (since Hine's preferred temperature was 25 °C) gives constant = 0.042 67. Therefore at 290 °C, τ_v = 0.04267(563.15) = 24.03. Substituting these values into eq 9 gives eq 13. This ΔG_{XY} gives K_{eq} = 2.09, which is

$$\Delta G_{XY} = D_Y - D_X + \tau_v(\sigma_X\sigma_{CH_2Y} - \sigma_Y\sigma_{CH_2X}) = -1.96 + 24.03(0.0472) = -0.826 \quad (13)$$

closer to the experimental values for **1b** and **1c**. Values of K_{eq} obtained with these additional corrections are listed in Table 1.

In addition to the considerations above, other factors may introduce some discrepancy between the calculated and observed values of K_{eq}. In the Cope rearrangement, the substituent allyl group that replaces a hydrogen present in Hine's condensed phase isomerization equilibria may introduce a variation in the entropy and energy changes involved. This should only occur if the effect were different in **1** and **2**, which seems unlikely. Also, the allyl substituent may alter the inherent "mixture of polar and resonance effects that controls interactions across a *trans* vinylene group."[12]

Hine also reported steric effects with alkylthio substituents. Replacement of hydrogen with allyl or β-methallyl could introduce such effects. However, these effects should be small since both isomers would be affected in roughly the same way.

In the cases of **1b** and **c**, a trace of aldehyde was present at the end of the rearrangement. Since precautions were taken to prevent hydrolysis of the enol ether products in the NMR solvent, crotonaldehyde is presumably produced at the rearrangement temperature. It is not known whether **1b**,**c** or **2b**,**c** or both produce the aldehyde. Therefore, the effect on the K_{eq} is unknown. Fortunately, the quantity of aldehyde is quite small.

Finally, **1e**,**f** and **1g-i**, prepared by Wittig olefination, were *E*/*Z* mixtures. The *trans* vinylene interactions should be different in the *Z* isomer. The *Z* isomer does seem to react faster. However, this should not affect the position of the final equilibrium, since presumably the *Z* isomer rearranges to the *E* form under the reaction conditions (*vide infra*).

Note that, in the carbamate series **1g-i**, reduction of nitrogen's π-donating character does indeed produce a reordering of the equilibrium directing ability of the groups, $N(CH_3)_2 > OCH_3 > N(CH_3)CO_2Et > CH_3 > H$, as postulated. Hine did not report *D* values for the

(10) Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480.
(11) Ratcliff, R.; Rodehorst, R. *J. Org. Chem.* **1970**, *35*, 4000.
(12) Hine, J.; Flachskam, N. W. *J. Am. Chem. Soc.* **1973**, *95*, 1179.
(13) Since the precise values used for the Hammet parameters were not obvious in Hine's paper, we use eq 11 to find the value of the ($\sigma_X\sigma_{CH_2Y} - \sigma_Y\sigma_{CH_2X}$) term.

carbamoyl group, so no calculated ΔG_{XY} is given. No rearrangement is seen in the case of **1i**, as expected.

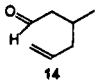
Are these rearrangements truly at equilibrium? Consider the case of **2b**:**1b**. Rearrangement at 320 °C in a sealed tube gave a K_{eq} of 1.5, similar in magnitude to that predicted using Hine's D values (3.45 or 1.92 corrected). However, rearrangement using a flow-through furnace gave a ratio of 0.67 at 420 °C. This suggested that **1b** was not in the tube long enough for equilibrium to be established, since Hine's D values at this temperature predict a K_{eq} of 2.86 (or 1.51 corrected). Therefore, the direction of isomerization was reversed starting with (*E*)-**2b**. The ratio of **2b**:**1b** in this direction was 1.5. The experimental equilibrium values ran about 0.5 lower than the corrected values calculated for the similar cases of **1b** and **1c** (see Table 1). At this temperature, an experimental K_{eq} of roughly 1 would be expected, indicating that neither **1b** nor **2b** has time to produce an equilibrium mixture in the flow-through furnace. On the other hand, these results suggest that the experimental value of 1.5 at 320 °C (sealed tube method) is likely to represent the equilibrium value.

In the nitrogen series, amino diene **1e** appears to rearrange to **2e** cleanly and completely at 300 °C. The K_{eq} is probably much greater than 50. Since a ratio as low as 50 could be easily detected by NMR, this number represents the lower limit of K_{eq} in this case. In contrast, the amino enol ether **1f** does not rearrange completely to **2f** at these temperatures. Apparently, the *Z* isomer of **1f** is more reactive than the *E* isomer. Rearrangement of (*Z*)-**1f** to (*E*)-**2f** was nearly complete after 15 min at 280 °C. The *E* isomer of **1f** was still present. Longer reaction times seem to promote decomposition. This contrasting behavior is in accord with the difference in D values between a CH_3 (**1e**) and a CH_3O (**1f**) substituent. The maximum predicted equilibrium constant in the case of **2e**:**1e** is 155; that predicted for **2f**:**1f** is 19. The reported value of 10 represents the ratio of (*E*)-**2f** to (*Z*)-**1f**. The true value must be larger. The calculated constants are consistent with the NMR results.

In the case of **1g**, the experimental K_{eq} of 23.5 at 20 min was unchanged (23.2) after 40 min at 290 °C. In the case of **1h**, equilibrium was approached more slowly. The K_{eq} value at 20, 40, and 80 min was 3.2, 9.3, and 16, respectively. A ratio of **2h**:**1h** = 3.2 at 20 min could, in the worst instance, indicate the passage of 2 half-lives if **1h** rearranges to **2h** irreversibly. Therefore, at 80 min (8 half-lives) a ratio of 256 would be expected. At 80 min, the experimental ratio was 16, indicating that equilibrium had been reached.[14]

In the case of **1i**, we postulated that no rearrangement would occur. Although experiment confirmed this hypothesis, we were concerned that a kinetic effect may have given similar results. The following experiments suggest that this was not the case. Heating (*Z*)-**1i** at 260 °C for 15 min gave a mixture of (*E*)- and (*Z*)-**1i** but no **2i**. Since rearrangement of **1h** was not complete for over 1 h, we thought that **1i** might show a similar (presumably steric) rate reduction. However, **1i** produced no **2i** even at 300 °C. The experimental protocol should have eliminated radical- or proton-catalyzed pathways for the *E*/*Z* isomerization. These experiments suggest that the *Z* to *E* isomerization may be occurring via Cope rearrangement but that the equilibrium strongly favors **1i**.

(14) Hydrolysis of the enamine **2h** gives the aldehyde **14** and unreacted **1h**. The ratio of **14** to **1h** is roughly the same as the **2h**:**1h** ratio, specifically, 7 at 40 min and 12 at 80 min (roughly estimated by ^{13}C NMR ratios of the CH_3 groups). This experiment confirms the identity of the enamine and supports the estimated K_{eq} of the Cope reaction.



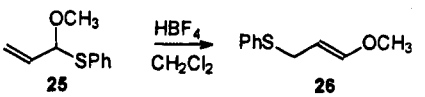
14

Table 2. Attempted Catalytic Cope Rearrangement. Substrates and Reaction Conditions

	amounts				reactn condns	
compd	substrate (mol, mg)	catalyst (mmol, mg)	THF (mL)	CH_3CN (mL)	*T* (°C)	reactn time (h)
1b	10, 50	1, 10	1.0	0	20	24
1b	10, 50	1, 10	no solvent		20	24
1b	10, 50	1, 10	2.0	0.6	reflux	1
1c	10, 50	1, 10	0	2.0	reflux	24
1c	10, 50	1, 10	1.0	0	reflux	24
1c	10, 50	2, 20	1.0	0	reflux	24
1c	10, 50	0.5, 5	0.5	0	reflux	96
1f	10, 50	1, 10	2.5	0	20	24

Other Substrates. Multiply substituted **15a** rearranged fairly cleanly to **16a**. In this case, the allylic system was substituted on both sides with a CH_3 group; thus, the system reduces to the case of CH_3O vs H. Replacing two hydrogens with a CH_3 group doubtless has varying steric, dipolar, and conjugative effects on the stability of the π bond, and hence, no simple additivity effect can be presumed. However, neglecting this, an experimental K_{eq} of at least 100 would be expected by this first-order analysis. In fact, the rearrangement appears to be complete.

We also expected **16b** to rearrange to **15b** and that **15c** would show little preference to rearrange to **16c**. Conjugation to oxygen should be preferred over conjugation to sulfur considering the relative magnitudes of the D values. The π-donating ability of CH_3O also seems to drive the equilibrium in the previously reported acid-catalyzed rearrangement of **25** to **26**.[15] This reaction was very rapid at low temperatures and irreversible.



25 **26** eq. 14

Unfortunately, attempts to force rearrangement of sulfides **15c** and **16b** in the gas phase (290 °C) led to decomposition.

Attempted Catalysis. Kirmse reported that the methylthio analogue of **15c** had a tendency to fragment in the gas phase.[2] The weaker bond strength of PhS–C compared to CH_3S–C may exacerbate the problem in the phenylthio case. We thought this difficulty could be overcome by Lewis acid catalysis of the rearrangement as reported by Overman.[16] Table 2 summarizes these experiments. Neither **1b**,**c**, nor **f** showed rearrangement with the palladium(II) catalyst. The intermediate suggested by Overman appears to require an electron-donating substituent on C2 or C5 of the diene. The absence of this feature in **1b** and **f** might explain their inertness. However, **1c**, bearing a donor (albeit a weak one), also does not rearrange. Serebryakov and Gamalevich have reported the rearrangement of oxygenated substrates; however, their substrates lead directly to ketones. In addition, they found that substituents at C2

(15) Hagen, J. P.; Harris, J. J.; Lakin, D. *J. Org. Chem.* **1987**, *52*, 782.

(16) Overman, L. E.; Jacobsen, E. J. *J. Am. Chem. Soc.* **1982**, *104*, 7225.

and C3 or at C3 *and* C5 were required for practically useful rearrangement.[17]

Conclusion

Hine's *D* values have semiquantitative predictive value in determining the position of equilibrium in Cope rearrangements. Reduction of the π-donating character of nitrogen (carbamoyl vs dimethylamino) does change the directing ability of the nitrogen substituent so that the aggregate order is $N(CH_3)_2 > OCH_3 > EtO_2CN(CH_3) > CH_3 > H$.

Experimental Section

NMR spectra were obtained at 200 MHz (50 MHz, ^{13}C) using $CDCl_3$ (with 0.03% TMS, Aldrich) as solvent. The $CDCl_3$ was passed through alumina just before use when hydrolytically sensitive samples (enol ethers and enamines) were involved. Analytical and preparative GC were effected on a Gow Mac (20% SE on 60/80 chromosorb P, 4 ft × 0.25 in. column, helium carrier gas, and flow rate of 40 mL/min). Ratios of geometric and regioisomers were determined by NMR. Preparative HPLC was done with a Merck Lobar Lichroprep Si 60 silica (40–63 μm) column. Reagents were obtained from Aldrich and solvents from Fischer unless otherwise specified. THF (Aldrich) was distilled from Na/benzophenone. Strong base and DIBALH reactions were run under a nitrogen atmosphere. Spectral and physical data were not necessarily obtained from the experimental run described.

Cope Rearrangements. Method A. Sealed Tubes. Kirmse's procedure was adapted.[2] Glass tubing (3mm/5mm ID/OD) was used to fashion ampules of 6–8 cm in length. These were deacidified by soaking in 1,1,1,3,3,3-hexamethyldisilazane overnight. After the tubes were dried under reduced pressure, a 5–20 mg sample was added. The sample was degassed with five freeze–thaw cycles in liquid N_2, sealed, and then placed in a hot furnace until equilibrium was achieved.

Cope Rearrangements. Method B. Flow through Tube Furnace. Larger amounts of the rearrangement products (0.5–1.0 g) were obtained as follows. Copper tubing (1 m) was coiled (3 cm o.d. coils over a 30 cm length) to fit into a cylindrical furnace. A thermocouple (E-type) was mounted in the center of the furnace. U-shaped glass tubing was connected to each end. The sample in the inlet tube was heated in an oil bath under a stream of nitrogen. Product was collected in the cold (liquid N_2) downstream tube.

1,5-Heptadien-4-ol (3). Alcohol **3** was prepared by the method of Henze, Allen, and Leslie.[18] To the Grignard reagent formed from allyl bromide (17.3 mL, 0.20 mol) and Mg (14.6 g, 0.60 mol) was added crotonaldehyde (15.7 mL, 0.19 mol). Workup with saturated aqueous NH_4Cl followed by distillation (Kugelrohr, 68.0–69.0 °C, 15 mm) gave a colorless oil (14.0 g, 66%): $n_D^{22} = 1.4556$; IR (neat, cm^{-1}) 3400, 1635, 1130; ^1H NMR δ 1.68 (dd, J = 6.2, 0.8 Hz, 3H), 1.94 (s, 1H), 2.32 (m, 2H), 4.12 (q, J = 6.4 Hz, 1H), 5.13 (m, 2H), 5.50 (ddq, J = 15.3, 6.0, 1.4 Hz, 1H), 5.75 (m, 2H); ^{13}C NMR δ 17.6, 41.9, 71.7, 117.9, 126.8, 132.9, 134.4. The product was carried on without further purification.

4-Methoxy-1,5-heptadiene (1b). This compound was prepared from **3** (2.22 g, 19.8 mmol) by the method of Johnstone and Rose.[19] Distillation (Kugelrohr, 80 - 90 °C, 45 mm) gave a colorless oil (1.65 g, 66%): $n_D^{22} = 1.4339$; IR (neat, cm^{-1}) 3460, 3070, 1670, 1640, 1090; ^1H NMR δ 1.73 (dd, J = 6.3, 1.5 Hz, 3H), 2.30 (m, 2H), 3.25 (s, 3H), 3.54 (dt, J = 8.0, 6.4 Hz, 1H), 5.08 (m, 2H), 5.31 (ddq, J = 15.3, 8.1, 1.5 Hz, 1H), 5.65 (m, 1H), 5.75 (ddt, J = 17.2, 10.3, 7.0 Hz, 1H); ^{13}C NMR δ 17.6, 40.1, 55.8, 82.0, 116.6, 129.0, 131.2, 134.8; MS m/z 126 (M^+), 125 ($M^+ - H$), 111 ($M^+ - CH_3$), 97 ($M^+ - C_2H_5$), 95 ($M^+ - OCH_3$), 85 ($M^+ - CH{=}CHCH_3$); HRMS (EI) calcd for $C_8H_{14}O$ 126.1045, found 126.1049.

2-Methyl-1,5-heptadien-4-ol (4). Following the method of Henze, Allen and Leslie,[18] 1-bromo-2-methyl-2-propene (12 g, 0.089 mol) was reacted with Mg (6.5 g, 0.27 mol) in 150 mL of ether. Crotonaldehyde (6.2 g, 0.089 mol) was added to the Grignard solution. Workup, followed by short-path distillation (90–108 °C, 52 mm), gave a colorless oil (4.8 g, 42%). Preparative GC (133 °C) gave **4** (t_R = 3.8 min): IR (neat, cm^{-1}) 3375, 1685, 1650, 1050; ^1H NMR δ 1.70 (dt, J = 5.5, 0.7 Hz, 3H), 1.77 (s, 3H), 1.77 (s, 1H), 2.22 (d, J = 6.5 Hz, 2H), 4.19 (q, J = 6.5 Hz, 1H), 4.84 (d, J = 14.1 Hz, 2H), 5.50 (ddq, J = 15.3, 6.5, 1.3 Hz, 1H), 5.72 (dq, J = 15.3, 6.3 Hz, 1H); ^{13}CMR δ 17.6, 22.4, 46.2, 66.9, 113.6, 126.7, 133.4, 143.3. The material was carried on without further purification.

4-Methoxy-2-methyl-1,5-heptadiene (1c). Following the method of Johnstone and Rose,[19] **4** (1.0 g, 7.9 mmol) was methylated. Workup, followed by short-path distillation (72–80 °C, 50 mm), gave a mixture of the starting material and **1c** as a colorless oil (0.82 g, 66% crude). Separation by HPLC (5% ether in hexane, flow rate = 3.00 mL/min) afforded **1c** (0.20 g, 15%, t_R = 12 min). Preparative GC (133 °C, t_R = 2.9 min) gave the analytical sample: IR (neat, cm^{-1}) 3075, 1671, 1647, 1100, 968, 889; ^1H NMR δ 1.71 (dd, J = 6.4, 1.5 Hz, 3H), 1.73 (s, 3H), 2.14 (dd, J = 14.0, 7.3 Hz, 1H), 2.33 (dd, J = 13.8, 5.9 Hz, 1H), 3.25 (s, 3H), 3.64 (q, J = 6.4 Hz, 1H), 4.75 (d, J = 11.1 Hz, 2H), 5.28 (ddq, J = 15.3, 8.1, 1.5 Hz, 1H), 5.58 (dq, J = 15.3, 6.3 Hz, 1H); ^{13}CMR δ 17.6, 22.8, 44.1, 55.8, 80.8, 112.3, 128.8, 131.4, 142.5. Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.08; H, 11.20.

1-Methoxy-3-methyl-1,5-hexadiene (2b). With method A, **1b** (10 mg, 320 °C, 30 min) gave a ratio of **2b**:**1b** of 1.5. With method B, **1b** (0.441 g, 420 °C) gave a ratio of **2b**:**1b** of 0.67 (0.392 g, 89%). Preparative GC (68 °C) gave a fraction containing allyl ether **1b** and (*Z*)-**2b** (71.2%, t_R = 12.8 min) and a fraction corresponding to (*E*)-**2b** (26.2%, t_R = 15.8 min). (*Z*)-**2b** (from mixture with **1b**): ^1H NMR δ 0.96 (d, J = 6.1 Hz, 3H), 2.08 (m, 2H), 2.70 (m, 1H), 3.56 (s, 3H), 4.19 (dd, J = 9.3, 6.3 Hz, 1H), 5.00 (obscured, 2H), 5.75 (obscured, 1H), 5.85 (obscured, 1H); ^{13}C NMR δ 20.7, 28.8, 41.8, 59.5, 112.7, 115.2, 137.5, 145.0. (*E*)-**2b**: IR (neat, cm^{-1}) 1640, 1113, 900; ^1H NMR δ 1.00 (d, J = 6.4 Hz, 3H), 2.13 (m, 3H), 3.50 (s, 3H), 4.60 (dd, J = 12.7, 7.8 Hz, 1H), 5.00 (m, 2H), 5.78 (dddd, J = 18.0, 8.5, 6.9, 6.8 Hz, 1H), 6.35 (d, J = 12.7 Hz, 1H); ^{13}C NMR δ 21.3, 32.7, 42.5, 55.9, 108.8, 115.6, 137.3, 146.2.

Thermal Isomerization of 2b to 1b. With method B, **2b** (6.5 mg, 412 °C), isolated by preparative GC as above, gave a ratio of **2b**:**1b** of 1.5.

1-Methoxy-3,5-dimethyl-1,5-hexadiene (2c). With method A, **1c** (10 mg, 290 °C, 15 min) afforded a mixture of **1c** and the *E* and *Z* isomers of **2c** (**2c**:**1c** = 1.4). With method B, **1c** (0.203 g, 415 °C) afforded an oil (0.13 g, 64%). GC (flow rate 60 mL/min, 100 °C) gave two fractions. The first fraction (70.1%, t_R = 4.8 min) contained a mixture of **1c** and (*Z*)-**2c**. The second fraction was (*E*)-**2c** (29.9%, t_R = 6.1 min). **1c**/(*Z*)-**2c**: IR ($CDCl_3$, cm^{-1}) 1649 weak; partial ^1H NMR ((*Z*)-**2c** in first fraction) δ 0.95 (d, J = 6.7 Hz, 3H), 1.68 (s, 3H), 1.98 (d, J = 7.3 Hz, 2H), 3.56 (s, 3H), 4.16 (dd, J = 9.2, 6.2 Hz, 1H), 5.82 (dd, J = 6.2, 0.96 Hz, 1H). The *Z* isomer of **2c** in the mixture was not detected in the ^{13}C NMR. (*E*)-**2c**: IR (neat, cm^{-1}) 1670, 1655, 937; ^1H NMR δ 0.97 (d, J = 6.7 Hz, 3H), 1.68 (s, 3H), 1.98 (d, J = 7.2 Hz, 2H), 2.25 (sept, J = 7.6 Hz, 1H), 3.49 (s, 3H), 4.66 (m, 3H), 6.28 (d, J = 12.7 Hz, 1H); ^{13}C NMR δ 21.4, 22.3, 30.7, 46.8, 55.8, 109.1, 111.7, 144.3, 145.9.

Ethyl 2-(*N*,*N*-Dimethylamino)-4-pentenoate (7). Allyl bromide (2.64 mL, 30.4 mmol) was added dropwise to a 4 °C solution of **5** (4.32 mL, 30.4 mmol) in CH_3CN (14 mL).[20] After 1 h at room temperature the solution was cooled to 4 °C, and potassium *tert*-butoxide (7.07 g, 63 mmol) in 80 mL of THF was added. After 15 min the mixture was diluted with ether (80 mL) and poured into 5% $NaHCO_3$. The aqueous layer was separated and then extracted twice with ether. The combined ether extracts were washed with brine, dried over $MgSO_4$, and filtered. The solvent was removed under reduced pressure to

(17) Serebryakov, E. P.; Gamalevich, G. D. *Izv. Akad. Nauk SSS, Ser. Khim.* **1987**, *1*, 132.

(18) Henze, H. R.; Allen, B. B.; Leslie, W. B. *J. Org. Chem.* **1942**, *7*, 328.

(19) Johnstone, R. A. W.; Rose, M. E. *Tetrahedron* **1979**, *35*, 2169.

(20) Razina, T. L.; Kocharyan, S. T.; Marukyan, T. Kh.; Galoyan, A. A.; Babayan, A. T. *Khim.-Farm. Zh.* **1983**, *17*, 916.

give a yellow oil. Short path distillation (88–90 °C, 30 mm) gave a colorless oil (1.94 g, 74%): IR (neat, cm^{-1}) 1745; ^1H NMR δ 1.28 (t, J = 7.1 Hz, 3H), 2.35 (s, 6H), 2.41 (m, 2H), 3.19 (dd, J = 8.1 Hz, 1H), 4.18 (q, J = 7.1 Hz, 2H), 5.10 (m, 2H), 5.78 (ddt, J = 17, 13.8, 6.8 Hz, 1H); ^{13}CMR δ 14.4, 34.2, 41.7, 60.1, 67.6, 117.2, 134.4, 171.7. An analytical sample was prepared by preparative GC. Anal. Calcd for $C_9H_{17}NO_2$: C, 63.13; H, 10.01; N, 8.18. Found: C, 62.98; H, 10.14; N, 8.09.

2-(*N,N*-Dimethylamino)-4-pentenal (8). Ester **7** (4.01 g, 23.4 mmol) was dissolved in hexanes (57 mL) and cooled to −65 °C. Dropwise addition of DIBALH (58.5 mL, 1 M in hexane) proceeded for 10 min with a 10–15 °C temperature increase during the first half of the addition. The temperature was increased to −40 °C for 1.5 h. The solution was diluted with ether while still cold and then immediately poured into 60 mL of rapidly stirred 10% v/v HCl. When the reaction ceased, the mixture was neutralized with 5% $NaHCO_3$. The resulting gelatinous layer was extracted three times with 250 mL ether, and the combined extracts were washed with brine, dried over $MgSO_4$, and filtered. The solvent was removed under reduced pressure to give crude **8** (3.85 g) which was carried on without further purification: ^1H NMR δ 2.39 (s, 6H), 2.45 (m, 2H), 2.95 (ddd, J = 7.6, 6.0, 2.1 Hz, 1H), 5.11 (m, 2H), 5.82 (ddt, J = 16.9, 9.9, 6.8 Hz, 1H), 9.67 (d, J = 2.1 Hz, 1H); ^{13}CMR δ 29.9, 42.4, 72.8, 117.6, 134.2, 203.4.

Wittig Procedure. Method A. *n*-Butyllithium (20.4 mL, 28.6 mmol, 1.4 M in hexane) was added dropwise to a 4 °C solution of the appropriate triphenylphosphonium salt (28.6 mmol) in 60 mL of THF. The resulting red solution was stirred for 30 min, and then the crude aldehyde (0.8 equiv) was added in THF (10 mL). The mixture was stirred for 15 h at 20 °C and then diluted with two volumes of water and 1 volume of dry ether. The layers were separated and the aqueous layer extracted three times with 30 mL portions of ether. The combined organic extracts were washed with 30 mL of brine and then dried over $MgSO_4$. The solvent was removed under reduced pressure to give the crude product.

Wittig Procedure. Method B. To the phosphonium salt (4.97 mmol) in THF (12 mL) at 4 °C was added *n*-butyllithium (2.13 mL, 4.97 mmol, 2.33 M in hexane) dropwise. The contents were stirred for at least 30 min. The aldehyde (4.77 mmol) was then added dropwise. The solution was stirred under nitrogen for 3 days at 20 °C. Workup was the same as method A.

4-(*N,N*-Dimethylamino)-1,5-heptadiene (1e). Method A. $C_2H_5PPh_3Br$ (14.7 g, 39.6 mmol) and **8** (5.65 g, 33.0 mmol) were used. Short path distillation (57–65 °C, 21 mm) gave a colorless oil (1.823 g, 33%): IR (neat, cm^{-1}) 1640, 910; ^1H NMR δ 1.64 (dd, J = 6.9, 1.8 Hz, 3H), 2.25 (s, 6H), 2.28 (m, 2H), 3.19 (dddd, J = 8.4, 8.3, 4.8, 0.74 Hz, 1H), 5.04 (m, 2H), 5.33 (m, 1H), 5.70 (m, 1H), 5.77 (ddt, J = 17.1, 14.1, 7.0 Hz, 1H); ^{13}CMR δ 13.5, 37.7, 41.8, 60.8, 116.2, 127.0, 129.2, 135.7. Preparative GC (152 °C, t_R = 2.4 min) gave the analytical sample. Retention time gradually decreased with replicate injections indicating decomposition on the column. Anal. Calcd for $C_9H_{17}N$: C, 77.63; H, 12.31; N, 10.06. Found: C, 77.23; H, 12.46; N, 9.83.

3-(*N,N*-Dimethylamino)-1-methoxy-1,5-hexadiene (1f). Method A. $Ph_3PCH_2OCH_3Cl$ (11.8 g, 31.92 mmol) and **8** (4.55 g, 26.6 mmol) were used. Short path distillation (82–89 °C, 24 mm) gave a colorless oil (1.12 g, 27%). Preparative GC (152 °C) gave two major peaks (t_R = 1.25, 1.64 min). The colorless sample injected had turned yellow on the column. The second fraction showed no enolic protons by NMR. NMR of the first peak showed a trace of the impurity but no separation of the *E*/*Z* isomers of **1f**: IR (neat, cm^{-1}) 3080, 1640, 910, 800, 750, 645; ^1H NMR δ 2.21 (two s, 6H), 2.25 (m, 2H), 2.73 (m, 2H), 3.54 (s, 3H, (*E*)-OMe), 3.57 (s, 3H, (*Z*)-OMe), 4.26 (dd, J = 9.8, 6.4 Hz, 1H, (*Z*)-C*H*CHO), 4.60 (dd, J = 12.7, 9.5 Hz, 1H, (*E*)-C*H*CHO), 5.03 (m, 2H), 5.77 (m, 1H), 6.06 (dd, J = 6.4, 0.83 Hz, 1H, (*Z*)-C*H*O), 6.34 (d, J = 12.7 Hz, 1H, (*E*)-C*H*O). (*E*)-**1f**: ^{13}C NMR δ 38.3, 41.1, 55.6, 63.6, 99.9, 115.7, 135.6, 149.2. (*Z*)-**1f**: partial ^{13}C NMR δ 37.8, 41.6, 58.1, 67.3, 104.2, 115.4, 135.5, 147.9.

1-(*N,N*-Dimethylamino)-3-methyl-1,5-hexadiene (2e). Aminodiene **1e** (30 mg, in two sealed tubes) was heated at 280 °C for 15 min. Preparative GC (159 °C) gave **2e** (t_R = 2.4 min): IR (neat, cm^{-1}) 1720, 1650, 1080, 910; ^1H NMR δ 0.98 (d, J = 6.4 Hz, 3H), 2.19 (m, 3H), 2.53 (s, 6H), 4.13 (dd, J = 13.8, 7.3 Hz, 1H), 5.00 (m, 2H), 5.79 (m, 1H), 5.87 (dd, J = 13.8, 0.65 Hz, 1H); ^{13}C NMR δ 21.8, 34.8, 41.0, 43.2, 106.3, 115.4, 138.0, 138.7. The aldehyde hydrolysis product is a minor impurity: ^{13}C NMR δ 19.9, 28.0, 38.8, 50.3, 117.0, 136.2, 202.7.

1-(*N,N*-Dimethylamino)-3-methoxy-1,5-hexadiene (2f). Aminodiene **1f** (30 mg, in two sealed tubes) was heated at 280 °C for 15 min. ^1H NMR showed the appearance of characteristic (*E*)-**2f** absorptions at δ 3.98 (dd, J = 13.7, 8.5 Hz) and δ 5.82 (d, J = 13.6 Hz). Decomposition was indicated by the presence of CH_3OH and $HN(CH_3)_2$ singlets. The absorptions of (*Z*)-**1f** were nearly absent but those of (*E*)-**1f** remained. The ratio of (*E*)-**2f** to (*E*)-**1f** was 10.

***N*-(Ethoxycarbonyl)sarcosine, Ethyl Ester (10).** To ester **9** (25.43 g, 0.166 mol, Lancaster) in ether (140 mL) was added ethyl chloroformate (20.9 mL, 0.212 mol, 97%). The mixture was then cooled to 4 °C. Water (20 mL) was added, and then aqueous NaOH (14.54 g, 0.356 mol, in 80 mL of water) was immediately added dropwise with rapid mechanical stirring over 7 min. At the end of the addition period, the bath was removed and the mixture was stirred for another 10 min. The layers were separated. The water layer was extracted twice with 50 mL portions of ether. The combined ether layers were washed with brine and then dried over $MgSO_4$. The ether was removed by rotatory evaporation and the residue then distilled (140–144 °C, 38 mm) to give a colorless oil (28.9 g, 92%): IR (neat, cm^{-1}) 1751, 1707; ^1H NMR δ 1.23 and 1.28 (t, J = 7.1 Hz, and t, J = 7.2 Hz, 6H), 2.97 and 2.98 (two s, 3H), 3.96 and 4.02 (two s, 2H), 4.12 (m, 2H), 4.21 (q, J = 7.1 Hz, 2H); ^{13}C NMR δ 169.3, 156.6, 156, 61.4, 61.3, 60.7, 50.3, 35.5, 34.8, 14.3, 13.9. Anal. Calcd for $C_9H_{17}NO$: C, 50.78; H, 7.99; N, 7.40. Found: C, 50.38; H, 8.04; N, 7.28.

Ethyl 2-(*N*-(Ethoxycarbonyl)-*N*-methylamino)-4-pentenoate (11) and Ethyl 2-Allyl-2-(*N*-(ethoxycarbonyl)-*N*-methylamino)-4-pentenoate (12). To $HN[Si(CH_3)_3]_2$ (35.28 mL, 0.167 mol) at −78 °C was added THF (105 mL), *n*-BuLi (71.8 mL, 2.33 M in hexane), and then **10** (28.8 g, 0.152 mol) in THF (8 mL). The flask was warmed to 20 °C over 10 min and then allowed to stand for another 20 min during which time a yellow color developed. The flask was then returned to the −78 °C bath. After 35 min in the bath, neat allyl bromide (14.5 mL, 0.167 mol) was added over 7 min. The bath was then removed and the solution allowed to stand for 1.75 h. The now orange solution was poured into HCl (200 mL, 1 M) and ether (250 mL). The separated ether phase was washed sequentially with equal volumes of H_2O, $NaHCO_3$, and brine and then dried over $MgSO_4$. The solvent was removed under reduced pressure and the residual oil (31.83 g) fractionally distilled (14 cm glass helices). Three fractions of **11** (15.4 g, 82–94 °C, 32 mm) were collected. Each contained increasing amounts of **12** (4, 10, and 16%). Two additional fractions (4.0 g, 94–115 °C, 32 mm) contained **12** and other impurities. The first three fractions were combined and then redistilled to give a first fraction of **11** (4.0 g, 89–103 °C, 32 mm) free of **12**. GC (214 °C, 50 mL/min) gave the analytical samples. **11** (t_R = 3.0 min): IR (neat, cm^{-1}) 3080, 1740, 1700, 1640, 920, 770; ^1H NMR δ 1.20 (t, J = 7.1 Hz, 6H), 2.55 (m, 2H), 2.84 and 2.88 (two s, 3H), 4.15 and 4.19 (two overlapping q, J = 7.0 Hz, 4H), 4.62 (dd, J = 10.6, 5.0 Hz, 0.44 H), 4.87 (dd, J = 10.6, 5.0 Hz, 0.58H), 5.10 (m, 2H), 5.73 (m, 1H); ^{13}C NMR δ 14.0, 14.4, 30.2, 31.0, 33.1, 33.4, 57.9, 58.4, 61.0, 61.5, 117.5, 117.7, 133.7, 157.0, 157.4, 171.0. Anal. Calcd for $C_{11}H_{19}NO_4$: C, 57.63; H, 8.35; N, 6.11. Found: C, 57.43; H, 8.25; N, 5.99. **12** (t_R = 5.2 min): IR (neat, cm^{-1}) 3075, 1735, 1690, 1635, 915, 765; ^1H NMR δ 1.24 (t, J = 7.1 Hz, 3H), 1.25 (t, J = 7.1 Hz, 3H), 2.56 (dd, J = 13.8, 7.6 Hz, 2H), 2.81 (dd, J = 13.7, 6.8 Hz, 2H), 2.96 (s, 3H), 4.15 and 4.12 (two overlapping q, J = 7.0 Hz, 4H), 5.13 (m, 4H), 5.70 (ddd, J = 16.7, 14.6, 7.3 Hz, 2H); ^{13}C NMR δ 14.1, 14.4, 31.0, 37.8, 60.7, 61.3, 65.5, 119.2, 132.2, 156.0, 172.4. Anal. Calcd for $C_{14}H_{23}NO_4$: C, 62.43; H, 8.61; N, 5.20. Found: C, 62.12; H, 8.63; N, 5.15.

2-(*N*-(Ethoxycarbonyl)-*N*-methylamino)-4-pentenal (13). To **11** (4.18 g, 18.2 mmol) in hexane (32 mL) at −70 °C was added DIBALH (21.9 mL, 21.89 mmol, 1 M in hexane)

dropwise with stirring. The temperature was kept below −60 °C during the addition. The reaction was stirred for an additional 2 h and then poured into a beaker containing rapidly stirred HCl (1 M, 100 mL). The aqueous layer was extracted three times with 30 mL portions of ether. The combined organic layers were washed with saturated $NaHCO_3$ (70 mLs) and then brine. After the combined layers were dried over $MgSO_4$, the solvent was removed under reduced pressure. Distillation (Kugelrohr, 120 °C, 0.15 mm) gave colorless **13** (3.32 g, 98% crude). The aldehyde was used at once without further purification: IR (neat, cm^{-1}) 2983, 1736, 1690, 1200, 917; ^1H NMR δ 1.19 (two t, J = 6.9 Hz, 3H), 2.39 (m, 2H), 2.69 (m, 1H), 2.82 (s, 3H), 4.06 (q, J = 7.1 Hz, 2H), 5.06 (m, 2H), 5.70 (m, 1H), 9.54 (s, 1H); ^{13}C NMR δ 13.72, 14.4, 30.6, 32.6, 61.3, 65.5, 117.0, 117.9, 133.2, 133.5, 159.6, 199.0.

***N*-(Ethoxycarbonyl)-*N*-methyl-1,5-hexadien-3-amine (1g).** Using method B, Ph_3PCH_3Br (3.61 g, 10.1 mmole, 98%) was converted to the ylide during a 3 h period at 4 °C. Aldehyde **13** (1.61 g, 8.68 mmol) was then added, and stirring was continued for an additional 0.5 h and then another 1 h at 20 °C before workup. Rapid distillation (Kugelrohr, 100−140 °C, 0.1 mm) followed by slow distillation (Kugelrohr, 82−100 °C, 0.1 mm) gave a colorless oil (0.690 g). Preparative GC (174 °C, t_R = 3.2 min) gave a colorless oil with a trace of **13**. Satisfactorily pure samples were prepared by reinjection of the preparative material at lower temperature (136 °C, t_R = 10.0 min): IR (neat, cm^{-1}) 3081, 1670, 1644, 994, 920, 771; ^1H NMR δ 1.26 (t, J = 7.1 Hz, 3H), 2.34 (m, 2H), 2.72 (broad s, 3H), 4.14 (q, J = 7.1 Hz, 2H), 4.75 (broad m, 1H), 5.10 (m, 4H), 5.74 (m, 1H), 5.78 (ddd, J = 15.7, 10.7, 5.0 Hz, 1H); ^{13}C NMR δ 14.7, 28.5, 35.5, 56.5, 61.2, 116.1, 117.1, 134.6, 136.5, 156.8. Anal. Calcd for $C_{10}H_{17}NO_2$: C, 65.54; H, 9.35; N, 7.64. Found: C, 65.67; H, 9.45; N, 7.57.

***(E)*- and *(Z)*-*N*-(Ethoxycarbonyl)-*N*-methyl-1,5-heptadien-4-amine (1h).** Using $Ph_3PCH_2CH_3Br$ (3.75 g, 10.1 mmol, 99%) and **13** as described for **1g** gave **1h** as a colorless oil (1.03 g). Preparative GC (182 °C, t_R = 3.7 min) gave material suitable for Cope rearrangements and analysis. Analysis at a lower termperature (141 °C) gave partial separation of the two isomers (7/1, t_R major = 16.8 min, t_R minor = 18.6 min): IR (neat, cm^{-1}) 1698, 1643, 995, 915, 888, 852, 821, 770, 741, 668, 641, 600; ^1H NMR δ 1.26 (t, J = 7.1 Hz, 3H), 1.67 (dd, J = 6.4, 1.7 Hz, 3H), 2.28 (m, 2H), 2.74 and 2.71 (two singlets, 3H), 4.14 (q, J = 7.1 Hz, 2H), 5.06 (m, 3H), 5.37 (m, 1H), 5.65 (m, 2H); ^{13}C NMR major isomer δ 13.5, 14.7, 28.5, 37.5, 51.4, 61.1, 117.0, 128.3, 134.7, 158.7; minor isomer δ 17.8, 36.2, 56.0, 116.9, 127.5, 129.3, 135.0. Anal. Calcd for $C_{11}H_{19}NO_2$: C, 66.97; H, 9.71; N, 7.10. Found: C, 67.23; H, 10.10; N, 7.00.

***(E)*- and *(Z)*-*N*-(Ethoxycarbonyl)-*N*-methyl-1-methoxy-1,5-hexadien-3-amine (1i).** Method B was employed using $Ph_3PCH_2OCH_3Cl$ (1.704 g) and **13** (0.883 g, 4.77 mmol). Distillation (Kugelrohr 78 °C, 0.1 mm) gave a yellow oil (0.603 g, 51%). TLC (silica gel, 40% ether/hexanes) showed three spots (R_f = 0.84, 0.55, and 0.18). The crude reaction mixture (0.439 g) was purified by HPLC, giving an uncharacterized oil (t_R = 43.2 min, 0.149 g), *(E)*-**1i** (56.4 min, 0.145 g), and *(Z)*-**1i** (74.8 min, 0.053 g). *(E)*-**1i**: IR (neat, cm^{-1}) 1681, 1331, 1108, 911, 738; ^1H NMR δ 1.25 (t, J = 7.1 Hz, 3H), 2.29 (m, 2H), 2.73 (s, 3H), 3.52 (s, 3H), 4.13 (q, J = 7.1 Hz, 2H), 4.69 (m, 1H), 4.77 (dd, J = 7.6, 12.1 Hz, 1H), 5.06 (m, 2H), 5.71 (m, 1H), 6.46 (d, J = 11.7 Hz, 1H); ^{13}C NMR δ 14.6, 28.1, 37.3, 53.7, 56.0, 61.0, 101.2, 116.9, 134.8, 149.9, 156.4. *(Z)*-**1i**: IR (neat, cm^{-1}) 1693, 934, 735; ^1H NMR δ 1.25 (t, J = 7.1 Hz, 3H), 2.27 (m, 2H), 2.75 (s, 3H), 3.60 (s, 3H), 4.13 (q, J = 7.1 Hz, 2H), 4.38 (t, J = 6.3 Hz, 1H), 5.00 (m, 2H), 5.08 (m, 1H), 5.46 (m, 1H), 5.94 (d, J = 6.3 Hz, 1H). ^{13}C NMR δ 14.7, 29.3, 37.6, 50.9, 59.8, 60.9, 104.2, 116.5, 135.1, 147.9, 156.4.

***(E)*- and *(Z)*-*N*-Methyl-*N*-(ethoxycarbonyl)-1,5-hexadien-1-amine (2g).** Method A was used. Rearrangement of **1g** (8 mg, 290 °C, 40 min) to *(E/Z)*-**2g** was complete: IR ($CDCl_3$, cm^{-1}) 1661, 1641, 1015, 946, 926, 748, 737, 726, 712; ^1H NMR δ 1.30 (t, J = 7.1 Hz, 3H), 2.15 (m, 4H), 3.03 (s, 3H), 4.20 (q, J = 7.1 Hz, 2H), 4.82 (dt, J = 14.2, 6.8 Hz, 1H), 4.98 (m, 2H), 5.81 (ddt, J = 16.7, 10.3, 6.3 Hz, 1H), 7.03 and 6.90 (broad d, J = 14.4 Hz and broad d, J = 14.2 Hz, 1H); ^{13}C NMR δ 14.6, 29.7, 30.9, 34.7, 62.0, 108.4, 114.8, 128.1, 128.7, 138.2, 158.7.

***(E)*- and *(Z)*-*N*,3-Dimethyl-*N*-(ethoxycarbonyl)-1,5-hexadien-1-amine (2h) and Hydrolysis to 14.** Method A was used. Rearrangement of **1h** (12 mg, 290 °C, 80 min) gave a **2h**:**1h** ratio of 16: IR ($CDCl_3$, cm^{-1}) 1690, 1660, 1641, 1013, 926, 891, 748, 710, 646. *(E/Z)*-**2h**: ^1H NMR δ 1.03 (d, J = 6.5 Hz, 3H), 1.30 (t, J = 7.1 Hz, 3H), 2.08 (m, 2H), 2.26 (m, 1H), 3.02 (s, 3H), 4.20 (q, J = 7.1 Hz, 2H), 4.73 (dd, J = 14.3, 7.8 Hz, 1H), 5.02 (m, 2H), 5.76 (ddt, J = 16.0, 11.2, 7.0 Hz, 1H), 7.00 and 6.86 (broad d, J = 14.9 Hz and broad d, J = 14.3 Hz, 1H); ^{13}C NMR δ 14.6, 21.0, 30.9, 34.8, 42.3, 62.0, 114.7, 115.8, 127.4, 126.8, 137.1, 154.2; residual lines from starting material, 17.8, 28.5, 36.2, 51.4, 56.1, 61.1, 116.9, 117.0, 128.3, 129.3, 134.7, 134.9. Intentional hydrolysis of **2h** in the NMR tube resulted in a mixture of **14** and ethyl *N*-methylcarbamate. In the ^1H NMR the absorptions at δ 7.00 and 6.86 disappear as the aldehyde of **14** appears at δ 9.67 (t, J = 1.9 Hz, 1H).

Attempted Rearrangement of 1i. Method A. At 260 °C for 15 min, *(Z)*-**1i** gave a mixture of *(E)*- and *(Z)*-**1i** by NMR. At 300 °C for 15 min, *(E)*-**1i** showed no rearrangement to **2i** and no isomerization to *(Z)*-**1i**.

1,5-Heptadien-4-one (17) and 2,5-Heptadien-4-one (18). A sample of **3** (1.54 mL, 14 mmol) was converted to **17** via the method of Ratcliff and Rodehorst.[11] After distillation (Kugelrohr, 90.0−92.0 °C, 34 mm) a clear rose-tinted oil (1.24 g) was obtained. ^1H NMR revealed a mixture of **17**, **3**, and minor impurities. The material isomerized to **18** upon storage at −20 °C. Flash chromatography (ether:pentane, 1:9) gave **17** (0.62 g, 25%): n_D^{20} = 1.4611; IR (neat, cm^{-1}) 1665, 1640, 950, 920, 725; ^1H NMR δ 1.92 (dd, J = 6.8, 1.6 Hz, 3H), 3.34 (dt, J = 6.8, 2.7 Hz, 2H), 5.18 (m, 2H), 5.95 (ddt, J = 17.0, 10.3, 6.9 Hz, 1H), 6.16 (dq, J = 15.6, 1.7 Hz, 1H), 6.89 (dq, J = 15.7, 6.8 Hz, 1H); ^{13}CMR δ 18.2, 45.0, 118.5, 131.0, 131.2, 143.3, 197.8; of the previous literature reports for **18**,[21-23] the ^1H NMR agrees with Gibson and Erman; ^{13}C NMR δ 18.2, 130.1, 142.7, 189.1.

4-Methyl-1,5-heptadien-4-ol (19). CH_3Li (7.57 mL, 10.6 mmol, 1.4 M in Et_2O) was added dropwise to a stirred solution of **17** (0.583 g, 5.3 mmol) in dry Et_2O (106 mL) at 4 °C. The mixture was stirred 45 min and then quenched with saturated NH_4Cl (25 mL). The aqueous layer was extracted twice with ether. The combined extracts were washed with brine and then dried over $MgSO_4$. Evaporation of the solvent and distillation (Kugelrohr 90 °C, 38 mm) gave a clear colorless oil (0.46 g, 69%): IR (neat, cm^{-1}) 3380, 3080, 1630, 1100, 910, 730; ^1H NMR δ 1.26 (s, 3H), 1.64 (s, 1H), 1.70 (d, J = 5.2 Hz, 3H), 2.28 (m, 2H) 5.12 (m, 2H), 5.73 (m, 3H); ^{13}CMR δ 17.6, 27.7, 47.2, 71.8, 118.7, 122.9, 133.9, 137.6. The product was carried on without further purification.

4-Methoxy-4-methyl-1,5-heptadiene (15a). To **19** (0.26 g, 2.04 mmol) and freshly distilled methyl iodide (2.9 mL) was added silver oxide (0.76 g, 3.27 mmol) and crushed $CaSO_4$ pellets (0.74 g).[24] The mixture was heated at reflux for 65 h. MeI and Ag_2O were added every 10−12 h. The reaction was monitored by GC. The product mixture was filtered through a pad of Celite, and the MeI was removed under reduced pressure. Distillation (Kugelrohr 70−90 °C, 34 mm) gave a clear colorless oil (0.13 g, 45%). Preparative GC (102 °C, t_R = 5.2 min) gave samples suitable for subsequent Cope reaction and for analysis: IR (neat, cm^{-1}) 1630, 1070, 970; ^1H NMR δ 1.19 (s, 3H), 1.71 (dd, J = 6.1, 1.3 Hz, 3H), 2.29 (m, 2H), 3.15 (s, 3H), 5.05 (m, 2H), 5.38 (dq, J = 15.8, 1.3 Hz, 1H), 5.59 (dq, J = 15.7, 6.0 Hz, 1H), 5.79 (dddd, J = 19.9, 10.6, 9.3, 7.1 Hz, 1H); ^{13}C NMR δ 17.9, 21.8, 44.6, 49.9, 76.5, 117.3, 126.0, 134.4, 135.2. Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.11; H, 11.21.

(21) Gibson, T.; Erman, W. *J. Org. Chem.* **1972**, *37*(8), 1159.
(22) Snowden, R. L.; Linder, S. M.; Muller, B. L.; Schulte-Elte, K. H. *Helv. Chim. Acta* **1987**, *70*, 1858.
(23) Majetich, G.; Casares, A.; Chapman, D.; Behnke, M. *J. Org. Chem.* **1986**, *51*, 1745.
(24) Martin, S. F.; Reilgar, H.; Williamson, S. A.; Grzejsaczak, S. *J. Am. Chem. Soc.* **1987**, *109*, 6124.

6-Methoxy-4-methyl-1,5-heptadiene (16a) and Hydrolysis to 4-Methyl-6-hepten-2-one (24). With method A, **15a** (20 mg, 295 °C, 30 min) gave crude **16a** (20 mg). The NMR suggests impurities including methanol, 3-penten-2-one, and **24** from apparent hydrolysis. There was no indication of **15a** in the crude thermolysis product. Intentional hydrolysis in the NMR tube resulted in complete conversion of **16a** to **24**. Preparative GC (140 °C, t_R = 8 min) after hydrolysis gave **24**. The ^{1}H NMR agrees with that previously reported by Shono.[25] ^{13}C NMR δ: 19.7, 28.9, 30.5, 41.1, 50.3, 116.5, 136.6, 208.8.

3-(Phenylthio)propenal (21). This compound was prepared by the method of Engelhard and Kolb.[26]

1-(Phenylthio)-1,5-hexadien-3-ol (22). Using the method of Henze,[18] **21** (3.67g, 0.022 mmol) gave **22** as an orange oil (3.18 g): ^{1}H NMR δ 2.00 (s, 1H), 2.25 (m, 2H), 4.15 (q, J = 6.4 Hz, 1H), 5.07 (m, 2H), 5.75 (dd, J = 15.1, 6.5 Hz, 2H), 6.35 (dd, J = 15.1, 1.2 Hz, 1H), 7.28 (m, 5H); ^{13}C NMR δ 41.7, 71.3, 118.5, 124.5, 126.7, 129.0, 129.9, 133.7, 134.0, 134.7. Alcohol **22** was carried on without further purification.

1-(Phenylthio)-3-methoxy-1,5-hexadiene (16b). This compound was prepared from **22** (0.206 g, 1 mmol) by the Johnstone and Rose method.[19] Distillation (Kugelrohr, 92 °C, 0.45 mm) gave a yellow oil (0.132 g, 50%): ^{1}H NMR δ 2.35 (m, 2H), 3.31 (s, 3H), 3.68 (q, J = 6.6 Hz, 1H), 5.12 (m, 2H), 5.68 (dd, J = 15.2, 7.8 Hz, 2H), 5.79 (ddt, J = 16.3, 9.5, 7.0 Hz, 1H), 6.40 (d, J = 15.1 Hz, 1H), 7.28 (m, 5H). Since pilot attempts to rearrange **16b** failed, no further purification was attempted.

1-(Phenylthio)-2-butene (23). To KOH (9.13 g, 163 mmol) in DMSO (62 mL) was added thiophenol (4.2 mL, 40.7 mmol). The mixture was cooled to 6 °C, and crotyl chloride (4 mL, 40.6 mmol) in DMSO (6 mL) was added dropwise with stirring. Workup by the method of Johnstone and Rose[19] followed by distillation (Kugelrohr, 80–94 °C, 0.35 mm) gave a colorless oil (5.39 g, 81%): ^{1}H NMR δ 1.68 (d, J = 4.9 Hz, 3H), 3.52 (d, J = 5.9 Hz, 2H), 5.56 (m, 2H), 7.35 (m, 5H). The NMR also contains minor absorptions, presumably the Z-isomer: δ 1.58 (d, J = 4.7 Hz), 3.56 (d, J = 6.2 Hz). Sulfide **23** was carried on without further purification.

4-(Phenylthio)-1,5-heptadiene (15c). To N,N-diisopropylamine (9.91 mL, 69.5 mmol) in THF (46 mL) at −78 °C was added dropwise n-BuLi (45.9 mL, 69.0 mmol, 1.53 M in hexane) followed by **23** (3.8 g, 23.0 mmol). The mixture was stirred for 2 h. Allyl bromide (2.09 g, 24.2 mmol) was then added dropwise. After 10 min, H_2O was added and the layers were separated. The aqueous layer was extracted three times with ether. The combined ether extractions were dried over $MgSO_4$, filtered, and then reduced by rotatory evaporation. Distillation (Kugelrohr 90–103 °C, 0.25 mm) gave a colorless liquid (4.20 g, 89%). The product was purified by GC (176 °C) giving four fractions: t_R = 4.4 min, 4.6% (**23**); t_R = 8.4 min, 68% (**15c**); t_R = 10.8 min, 15% (isomeric compound); and t_R = 16.8 min, 12% (unidentified). The **15c** fraction contained about 20% of a probable geometric isomer: ^{1}H NMR δ 1.05 (d, J = 4.6 Hz, 3H), 2.41 (m, 2H), 3.61 (m, 1H), 5.10 (m, 2H), 5.33 (m, 2H), 5.83 (ddt, J = 16.5, 9.6, 7.3 Hz, 1H), 7.25 (m, 5H); ^{13}C NMR δ 17.6, 39.0, 51.1, 116.9, 127.0, 127.3, 128.6, 130.9, 133.0, 133.5, 135.3; MS m/z 244 (contaminant PhSS(=O)Ph?), 218 (contaminant PhSSPh?), 204 (M^+), 163 (M^+ − CH=CHCH$_3$); HRMS (EI) calcd for $C_{13}H_{16}S$ 204.0973, found 204.0974; MS (for t_R = 10.8 min material) m/z 203 (M^+ − H), 163 (M^+ − CH=CHCH$_3$); HRMS (EI) calcd for $C_{13}H_{15}S$ (M^+ − H) 203.0894, found 203.0892. Since pilot attempts to rearrange **15c** failed, no further purification was attempted.

Acknowledgment. We would like to thank the Research Corporation and the UNO Committee on Research for partial support of this project, Maria Hoffmann and Patrick McLaughlin for preliminary experiments, and Dr. James K. Wood for helpful discussions.

Supporting Information Available: Copies of spectra for compounds **1b,f,i, 2b,c,e-h, 3, 4, 8, 13, 14, 15c, 16a,b, 17, 19,** and **22–24** (26 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO950979K

(25) Shono, T.; Nishiguchi, I.; Ohmizu, H.; Mitani, M. J. *J. Am. Chem. Soc.* **1978,** *100,* 545.

(26) Engelhard, N.; Kolb, A. *Liebigs Ann. Chem.* **1964,** *673,* 136.