90791-86-9; **2** (R = $CH_2CH(CH_3)CH(CH_3)_2$, R′ = $(CH_2)_7CH_3$), 90791-87-0; **2** (R = CH_2CH_2Ph, R′ = $(CH_2)_7CH_3$), 90791-88-1; (*R*)-**2** (R = $CH(CH_3)CH_2CH_3$, R′ = $(CH_2)_3CH_3$), 90791-97-2; (*R*)-**2** (R = $CH(CH_3)CH_2CH_3$, R′ = $(CH_2)_5CH_3$), 90791-98-3; (*R*)-**2** (R = $CH(CH_3)CH_2CH_3$, R′ = $(CH_2)_6CH_3$), 90791-99-4; (*R*)-**2** (R = $CH(CH_3)CH_2CH_3$, R′ = $(CH_2)_8CH_3$), 90792-00-0; (*R*)-**2** (R = $CH(CH_3)CH_2CH_3$, R′ = Ph), 90898-31-0; (*R*)-**2** (R = $CH(CH_3)CH_2CH_3$, R′ = c-C_6H_{11}), 90792-01-1; **2** (R = c-C_5H_9, R′ = $CCH_2)_7CH_3$), 90791-89-2; (*R*)-**2** (R = $CH(CH_3)CH_2CH_3$, R′ = $(CH_2)_2CH_3$), 90822-56-3; (*R*)-**2** (R = $CH(CH_3)CH_2CH_3$, R′ = $C(CH_3)_3$), 90792-02-2; **3** (R′ = $(CH_2)_7CH_3$), 90791-85-8; **6**, 90865-48-8; **7**, 90822-55-2; Ipc_2BH, 21947-87-5; $CH_2{=}CH(CH_2)_3CH_3$, 592-41-6; $CH_2{=}C(CH_3)CH_2CH_3$, 563-46-2; $CH_2{=}C(CH_3)CH(CH_3)_2$, 563-78-0; $C_6H_5CH{=}CH_2$, 100-42-5; *cis*-$CH_3CH{=}CHCH_3$, 590-18-1; $CH{\equiv}C(CH_2)_7CH_3$, 764-93-2; I_2, 7553-56-2; $CH{\equiv}C(CH_2)_2CH_3$, 627-19-0; $CH{\equiv}C(CH_2)_4CH_3$, 693-02-7; $CH{\equiv}C(CH_2)_5CH_3$, 629-05-0; $CH{\equiv}C(CH_2)_6CH_3$, 3452-09-3; $CH{\equiv}C(CH_2)_8CH_3$, 2243-98-3; $C_6H_4C{\equiv}CH$, 536-74-3; $CH{\equiv}CC(CH_3)_3$, 917-92-0; $LiC{\equiv}C(CH_2)_7CH_3$, 21433-46-5; (*R*)-$CH_3CH_2CH(CH_3)(CH_2)_{10}CH_3$, 55253-05-9; (*R*)-$CH_3CH_2CH(CH_3)CH{=}CH(CH_2)_8CH_3$, 90792-03-3; disiamylborane, 1069-54-1; cyclopentene, 142-29-0; cyclohexylethyne, 931-48-6; lithium 1-decynyldiisopinocampheylhexylborate, 90822-39-2; lithium 1-decynyldiisopinocampheyl-2-methylbutylborate, 90791-72-3; lithium 1-decynyldiisopinocampheyl-2,3-dimethylbutylborate, 90791-73-4; lithium 1-decynyldiisopinocampheylphenethylborate, 90791-74-5; lithium 1-decynyldiisopinocampheyl-2(*R*)-butylborate, 90822-40-5; lithium 1-decynyldiisopinocampheylcyclopentylborate, 90791-75-6; disiamylhexylborane, 16413-17-5; disiamyl-2-methylbutylborane, 90791-95-0; disiamyl-2-butylborane, 90791-96-1; lithium 1-decynyldisiamylhexylborate, 90791-76-7; lithium 1-decynyldisiamyl-2-methylbutylborate, 90791-77-8; lithium 1-decynyldisiamyl-2-butylborate, 90791-78-9; lithium 1-pentynyldiisopinocampheyl-2(*R*)-butylborate, 90791-79-0; lithium 1-hexynyldiisopinocampheyl-2(*R*)-butylborate, 90791-80-3; lithium 1-octynyldiisopinocampheyl-2(*R*)-butylborate, 90791-81-4; lithium 1-nonynyldiisopinocampheyl-2(*R*)-butylborate, 90791-82-5; lithium 1-undecynyldiisopinocampheyl-2(*R*)-butylborate, 90791-83-6; lithium phenylethynyldiisocampheyl-2(*R*)-butylborate, 90822-41-6; lithium cyclohexylethynyldiisocampheyl-2(*R*)-butylborate, 90822-42-7; lithium 1-(3,3-dimethylbutynyl)diisocampheyl-2(*R*)-butylborate, 90791-84-7.

An Investigation of the Intramolecular Ene Reaction of *N*-Acyl Imines[1]

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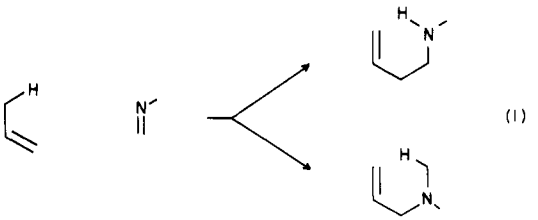
N-Acyl imines, produced by the flash vacuum thermolysis of hydroxamic acid derivatives, participate in the intramolecular ene reaction to give nitrogen heterocycles. The reaction is accelerated by carboxyl substitutents on the carbon atom of the *N*-acyl imine, and the reaction is more successful for the production of pyrrolidine rather than piperdine derivatives.

The ene reaction[2] was first described by Alder and coworkers[3] over 40 years ago. Although related to the Diels–Alder reaction, the ene reaction has been the focus of far fewer studies. Interest in the ene reaction has intensified in recent years resulting in a number of studies concerned with its mechanism[4] as well as its application to the solution of synthetic problems.[5]

The ene reaction using an imine as an enophile, in principle, has potential for the preparation of organic nitrogen compounds. It is also more complicated since there are two isomeric pathways that this reaction can follow. This is, the process can result in either the formation of a carbon–carbon or a carbon–nitrogen single bond (eq 1). From an analysis of the bond energies involved, both of these ene reactions involving imines are



(1)

predicted to be considerably less favorable than the all carbon ene reaction.[6] This situation is primarily a result of the small difference in bond strength between a C=N π bond and the nitrogen σ bonds, C–N and N–H, compared to a C=C π bond and the carbon σ bonds, C–C and C–H. Between the isomeric ene reaction of imines, bond energy data predict the pathway involving the formation of the carbon–nitrogen bond to be less favorable than formation of the carbon–carbon bond. The literature is consistent with this analysis. Simple imines, in contrast to either alkenes or even carbonyl compounds,[2,8] do not

(1) A preliminary account of a portion of this work has previously appeared: Koch, K.; Lin, J.-M.; Fowler, F. W. *Tetrahedron Lett.* **1983**, 1581.

(2) For reviews of the ene reaction, see: (a) Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 566. (b) Keung, E. C.; Alper, H. *J. Chem. Educ.* **1972**, *49*, 97. (c) Oppolzer, W.; Snieckus, V. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 476. (d) Snider, B. B. *Acc. Chem. Res.* **1980**, *13*, 426. (e) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 876.

(3) Alder, K.; Pascher, F.; Schmitz, A. *Ber. Dtsch. Chem. Ges.* **1943**, *76*, 27.

(4) For examples, see: (a) Oppolzer, W.; Sohail, M. *Helv. Chem. Acta* **1984**, *67*, 730. (b) Kwart, H.; Brechbiel, M. W. *J. Org. Chem.* **1982**, *47*, 3355; (c) **1982**, *47*, 5409. (d) Stephenson, L. M.; Orfanopoulos, M. *J. Org. Chem.* **1981**, *46*, 2200. (e) Jenner, G. *Bull. Soc. Chim. Fr.* **1984**, 275. (f) Inagaki, S.; Fujimoto, H.; Fukui, K. *J. Am. Chem. Soc.* **1976**, *98*, 4693.

(5) For examples, see: (a) Ogawa, Y.; Shibasaki, M. *Tetrahedron Lett.* **1984**, 1067. (b) Wovkulich, P. M.; Batcho, A. D.; Uskokovic, M. R. *Helv. Chem. Acta* **1984**, *67*, 612. (c) Snider, B. B.; Cartaya-Marin, C. P. *J. Org. Chem.* **1984**, *49*, 1688. (d) Salomon, M. F.; Pardo, S. N.; Salomon, R. G. *J. Am. Chem. Soc.* **1984**, *106*, 3797. (e) Oppolzer, W. *Pure Appl. Chem.* **1981**, *53*, 1181.

(6) The values (kcal/mol) for the bond energies used were: C–H (98), N–H (92),[7a] and C–C (83); C–N (72.8)[7b] and C=C (59.4); C=N (74.3) (π bond strengths).[7c] Estimates in kcal/mol for the enthalpies of the ene reactions are: the all carbon (–23.6) and the imine, C–C bond formation (–3.7) and the imine, C–N bond formation (+1.5).

(7) (a) Kerr, J. A. *Chem. Rev.* **1966**, *66*, 465. (b) Sandorfy, C. In "The Chemistry of the Carbon–Nitrogen Double Bond"; Patai, S., Ed.; Wiley-Interscience: New York, 1970; p 1. (c) Shaw, R. In "The Chemistry of Double Bonded Functional Groups"; Patai, S., Ed.; Wiley: New York, 1977; p 131.

(8) This trend has also been observed in the Diels–Alder reaction; that is, compared to both alkenes and carbonyl groups, imines are reluctant to participate in this reaction. This observation is also consistent with an analysis of the bond strengths involved. Primarily, the problem is that the energy difference between the π bond and σ bonds involving nitrogen are smaller than those involving either carbon or oxygen.

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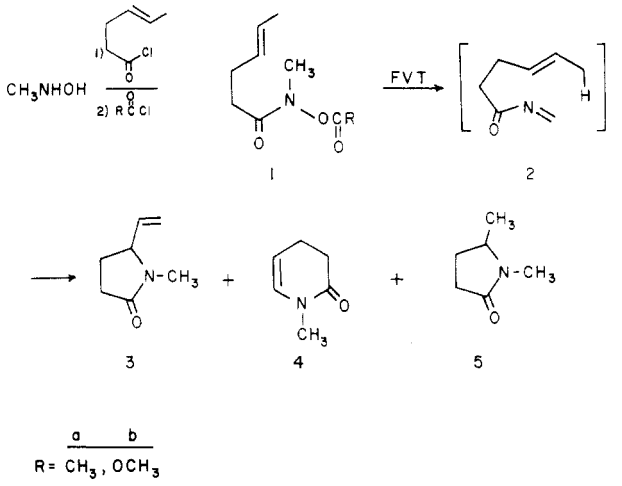
participate in the ene reaction. However, the retro-ene reaction of allyl amines to give imines and alkenes is well-known.[9] Successful ene reactions have only been reported for strained imines,[10] iminium ions,[11] and a few *N*-sulfonyl imines.[12] The regiochemistry of these reactions is also predicted by the above bond energy analysis. All of these examples of the ene reaction result in the formation of a carbon–carbon in preference to a carbon–nitrogen bond.

We have recently developed a synthesis of *N*-acyl-1-azadienes and studied their Diels-Alder reactivity.[13] Due to our success with these studies we were led to explore other pericyclic processes.[14] *N*-Acyl imines are suitable candidates for the ene reaction of carbon–nitrogen double bonds. The ene product is an amide with an associated stabilization of 15–20 kcal/mol providing an additional thermodynamic driving force for this reaction.[15] Since the amide should be partially formed in the transition state this factor should also lower the activation energy and accelerate the ene reaction. In addition, the greater electronegativity of the acyl function should further lower the LUMO of the imine, thus facilitating any HOMO–LUMO interactions in the transition state.[4f]

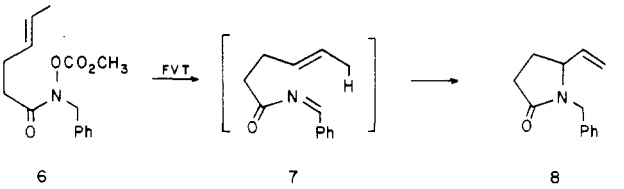
Hydroxamic acid derivative **1**, prepared from *N*-methylhydroxylamine, when evaporated through a hot tube gave the ene adduct **3** (40%) as the major product. Two additional products, **4** (15%) and **5** (15%), were also isolated. Although the structures of these compounds



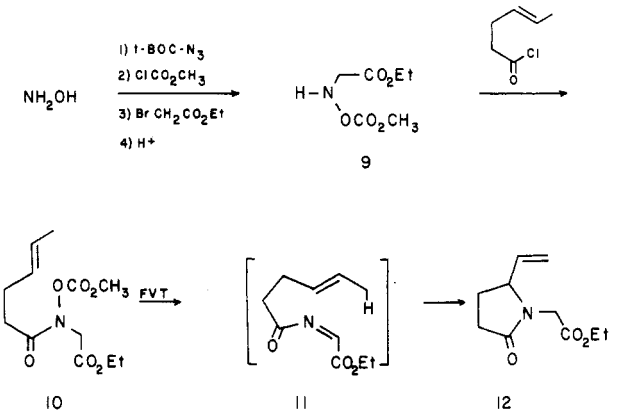
appear secure, the pathway for their formation is not obvious. Both of these compounds contain one carbon atom *less* than the ene product. The formation of these latter compounds was suppressed by preparing the *N*-acyl imine by using a carbonate rather than the acetate derivative of the hydroxamic acid. The carbonate derivative allows for the formation of the *N*-acyl imine at a lower temperature.

The transformation of **2**[16] to **3** represents one of the few examples of the ene reaction of an imine. It is the first example of an *N*-acyl imine behaving as an enophile[10–12] as well as the first example of this reaction proceeding to form a carbon–nitrogen single bond. The latter process is of interest because of its potential in heterocyclic synthesis.[17]

Phenyl substitution of the hydroxamic acid derivative **6** resulted in a lowering of the temperature required to produce the *N*-acyl imine. Unfortunately, this substitution also suppressed the enophilicity of the *N*-acyl imine, and only a 9% yield of the pyrrolidine **8** was observed.



A dramatic effect on the ene reaction was observed when the carbon atom of the imine carried an ester substituent. The formation of the *N*-acyl imine **11** from **10** as well as its ene reaction occurred at about 150–200° lower than that of **2**, and the yield of the ene reaction was higher. Since



the formation of the *N*-acyl imine can be considered a retro-ene reaction, the rate acceleration due to the ester group on both the formation of the acyl imine as well as its ene reaction can be attributed to an increased HOMO–LUMO interaction between the ene and enophile in the activated complex.

Our preliminary results indicated that the intramolecular ene reaction has potential for the preparation of pyrrolidine derivatives. Expansion of this scheme to the preparation of piperidines was only moderately successful. Evaporation of the hydroxamic acid derivative **13** through the pyrolysis tube gave piperidine **15** as the major product but in only 7% yield. This result is consistent with other intramolecular ene reactions, that is, formation of six-membered rings is less favorable than five.[2]

Another restriction on this ene reaction is that it generally will not be successful if the *N*-acyl imine contains an α hydrogen. When this situation exists, a hydrogen shift to give the more stable enamide occurs. For example, the

(9) (a) Viola, A.; Locke, J. S. *J. Chem. Soc., Chem. Commun.* **1984**, 1429. (b) Cadogan, J. I. G.; Hickson, C. L.; McNab, H. *J. Chem. Res.* **1983**, 2247. (c) Earl, R. A.; Vollhardt, K. P. C. *Heterocycles* **1982**, *19*, 265.

(10) Hickey, D. M. B.; Moody, C. J.; Rees, C. W. *J. Chem. Soc., Chem. Commun.* **1982**, 1419.

(11) Cohen, T.; Onopchenko, A. *J. Org. Chem.* **1983**, *48*, 4531.

(12) (a) Tschaen, D. M.; Turos, E.; Weinreb, S. M. *J. Org. Chem.* **1984**, *49*, 5058. (b) Tschaen, D. M.; Weireb, S. M. *Tetrahedron Lett.* **1982**, 3015. (c) Achmatowicz, O.; Pietraszkiewicz, M. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2680. (d) Achmatowicz, O.; Pietraszkiewicz, M. *J. Chem. Soc., Chem. Commun.* **1976**, 484.

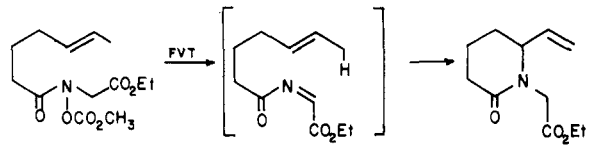
(13) Cheng, Y.-S.; Lupo, A.; Fowler, F. W. *J. Am. Chem. Soc.* **1983**, *105*, 7696.

(14) We have recently developed a new synthesis of 1,2-dihydropyridines based on an electrocyclic reaction of *N*-acyl-1-azatrienes (Wyle, M.; Fowler, F. W. *J. Org. Chem.* **1984**, *49*, 4025) as well as developing the 1-aza Cope reaction of *N*-acyl-1-aza 1,5-dienes.

(15) The rotational barriers suggest that there is only a small stabilizing interaction between the carbonyl group and the nitrogen lone pair of electrons in the *N*-acyl imine (Allmann, R.; Kupfer, R.; Nagel, M.; Wurthwein, E.-U. *Chem. Ber.* **1984**, *117*, 1597).

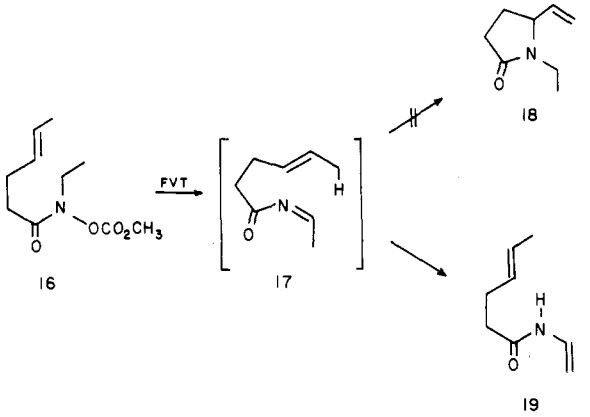
(16) The existence of *N*-acyl imines is inferred from trapping experiments using methanol (see ref 13).

(17) The intramolecular ene reaction of *N*-acyl azo (Vedejs, E.; Meier, G. P. *Tetrahedron Lett.* **1979**, 4185) and nitroso compounds (Keck, G. E.; Webb, R. R.; Yates, J. B. *Tetrahedron* **1981**, *37*, 4007) accomplish similar synthetic goals.



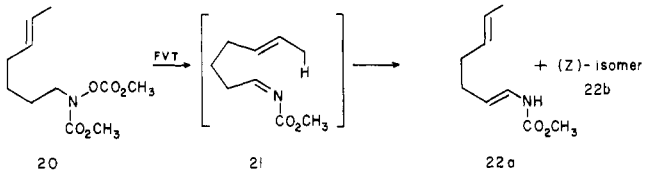
13 14 15

flash vacuum thermolysis of **16** gave an 85% yield of the enamide **19**. None of the ene product **18** could be detected.

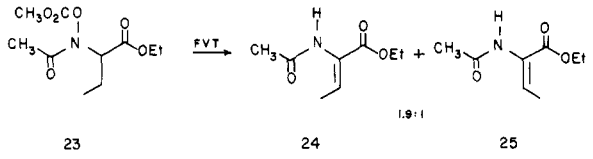


16 17 18 19

The carbamoyl imine **21**, which has the potential for undergoing the more favorable ene reaction (carbon–carbon bond formation), also rearranged to the enamide **22**. Since the yields of these reactions are high, this method provides a new synthesis of these enamides.[18] In fact, a special class of enamides, the dehydroamino acids,[19] (i.e., the conversion of **23** to **24** and **25**) are readily accessible with this method.[20]



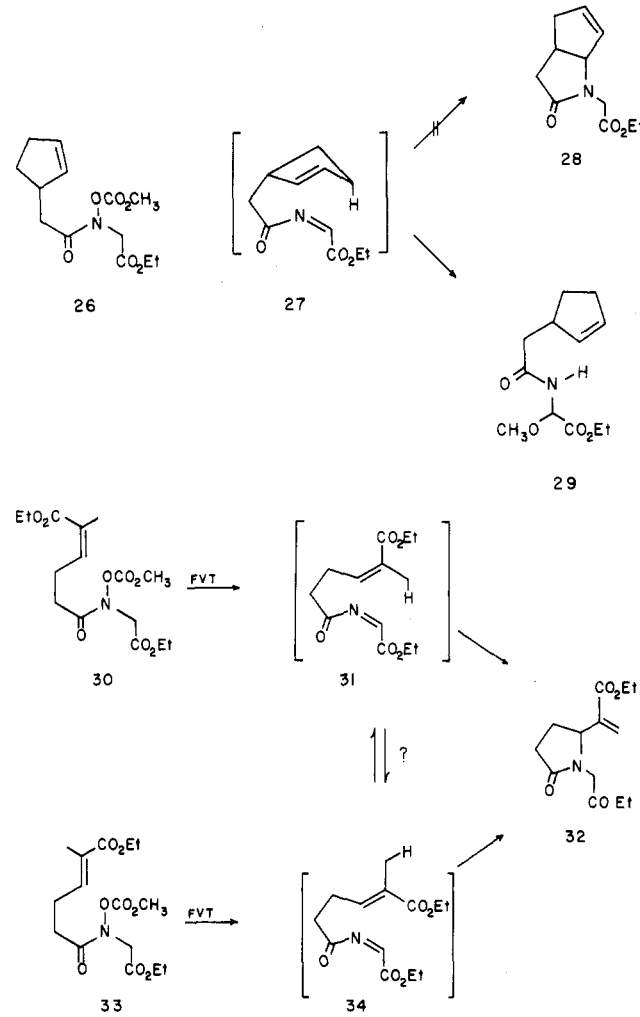
20 21 22a 22b



23 24 25

We were suprised to observe that *N*-acyl imine **27** failed to undergo the ene reaction. The product of this reaction would be a pyrrolidine, and an analgous all-carbon ene reaction is known.[21] The only product that could be isolated from this reaction was the carbinol amide **29**. This product was most likely produced by the addition of methanol, produced in the elimination process, to the *N*-acyl imine **27**.

Further insight into the question of ene geometry was obtained from the reaction of the isomeric acyl imines **30** and **33**. The *Z* isomer **31** (*trans*-ene) gave the ene product **32** in quantitative yield (greater than 90% pure). In



26 27 28 29 30 31 32 33 34

contrast, the *E* isomer 33 (*cis*-ene)gave a considerably more complex product mixture that, from NMR analysis, contained less than 25% of the ene product **32**. Both **27** and **33** are related in that they both posses *cis*-enes. The cis configuration of the ene effectively restricts the ene reaction to passing through an endo transition state.[22]

It is generally believed that the geometry of the ene has little effect on the ene reaction[23] of the all carbon systems. We believe the difference in reactivity of *N*-acyl imines may be due to the stabilizing effect of developing amide resonance energy in the activated complex. If a chairlike transition state is assumed[24] then inspection of molecular models indicates that the amide resonance will be greater in exo than endo reaction pathways (**35** and **36**, respectively). This is because the geometry of the ligands about

35 36

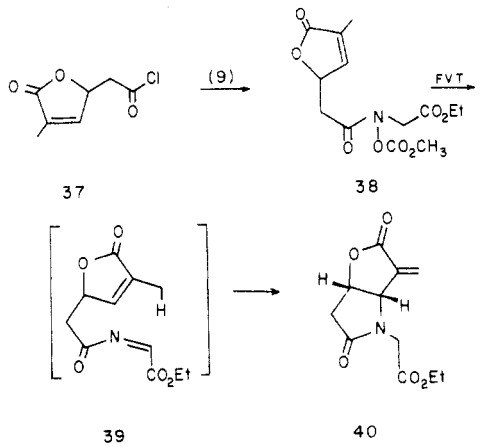
the nitrogen atom in the endo pathway does not allow for a favorable interaction between the carbonyl group and the developing lone pair of electrons. Basically, the p-

(18) Lenz, G. *Synthesis* **1978**, 489.
(19) Schmidt, U.; Hausler, J.; Ohler, E.; Poisel, H. *Fortschr. Chem. Org. Naturst.* 1979, *37*, 252.
(20) This synthesis of dehydroamino acids is similar to a base-catalyzed approach. For example, see: Herscheid, J.; Schotten, H.; Tijhuis, M.; Ottenheijm, H. Recl. *Trav. Chim. Pays-Bas* **1981**, *100*, 73.
(21) Oppolzer, W.; Pfenninger, E.; Keller, K. *Helv. Chem. Acta* **1973**, *56*, 1807.
(22) In order for the intramolecular ene reaction involving a *cis*-ene to follow an exo reaction pathway the six-membered ring transition state would be fused to the five-membered ring by using axial bonds. It is generally believed this would be higher in energy compared to other possible reaction pathways. For example, see ref 24.
(23) For example, see ref 1c, p 478.
(24) Oppolzer, W.; Mirza, S. *Helv. Chem. Acta* **1984**, *67*, 730.

atomic orbital component of the lone pair of electrons will develop along a pseudoequatorial direction in the endo reaction pathway whereas it will develop along a pseudoaxial direction in the exo reaction pathway. The lone pair in the pseudoaxial position will have a greater orbital overlap with the carbonyl group.

It is possible that the adduct **32** produced from **33** is a result of an *E* to *Z* isomerization of **34** to **31** rather than the direct ene reaction of **32**. This type of reactivity has previously been reported by Weinreb and co-workers.[12a] The failure to observe an ene product from **27** could be due to its inability to undergo a *Z* to *E* isomerization.

We were encouraged to observe that pyrrolidine **40** could be prepared from **39**. This α-methylene lactone as well as the acrylate **32** have potential as intermediates in natural product synthesis. It is interesting to note that these latter



37 38 39 40

ene reactions involve reaction partners that are both electron deficient. Although there are examples of both the diene and dienophile being electron deficient in the Diels–Alder reaction,[25] It is not a common situation in the ene reaction.[2]

In summary, the work described represent the first examples of *N*-acyl imines participating in the ene reaction as well as the first example of an ene reaction of an imine forming a carbon–nitrogen bond. The reaction is reasonably successful for the preparation of pyrrolidine derivatives. There are parallels between the intramolecular ene reaction of carbon–carbon and carbon–nitrogen double bonds. For example, they both work best for the formation of five-membered rings, and electron-withdrawing groups on the enophile accelerate the reaction. These results also suggest that the stereochemical requirements of the developing amide bond are important for estimating the relative energies of exo and endo reaction pathways of these ene reactions.

Experimental Section

General. Melting points were recorded on a Fisher-Johns melting point apparatus and are uncorrected. Infrared spectra were recorded on either a Perkin-Elmer 727 or a Perkin-Elmer 567 spectrometer as either thin films or KBr solid solutions. The absorption intensities were described as being either strong (s), medium (m), or weak (w) and were referenced to either the 1601.4- or the 1944-cm^{-1} absorption of polystyrene. Proton NMR spectra were recorded on either a Varian CFT-20 or a Nicolet NT-300 spectrometer. Carbon-13 NMR spectra were recorded on a Nicolet NT-300 spectrometer. All chemical shifts were reported in ppm from tetramethylsilane as an internal standard and described as being either singlet (s), doublet (d), triplet (t), quartet (q), quintet (q'), or multiplet (m). Low-resolution mass spectra (MS) were recorded on a Hewlett-Packard 5980A spectrometer. High-resolution mass spectra (HRMS) were recorded on a Kratos MS-30 spectrometer. Analytical gas chromatography (GC) was determined either on a Hewlett-Packard 5710A chromatograph or a Hewlett-Packard 5830 chromatograph equipped with a flame ionization detector. Preparative gas chromatography was carried out on a Varian 920 chromatograph equipped with a thermal conductivity detector. Thin-layer chromatography (TLC) was carried out with Anatech silica gel HLF precoated thin-layer chromatography plates. Flash column chromatography was carried out with 230–400 mesh silica gel 60 (E. Merck). Centrifugal thin-layer chromatography was performed on Harrison Research Inc. Chromatotron Model 7924. All dry solvents were distilled from sodium benzophenone ketyl under a nitrogen atmosphere. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN, or by Canadian Microanalytical Service Ltd., Vancouver, B.C., Canada.

***O*-Acetyl-*N*-(hex-4-enoyl)-*N*-methylhydroxylamine (1a).** In a 100-mL flask, 1.20 mmol of *N*-methylhydroxylamine hydrochloride was mixed with 2.39 mmol of anhydrous sodium carbonate in 50 mL of ether and was cooled in an ice bath for 5 min. To this mixture was added 10 mL of ether solution containing 1.20 mmol of hex-4-enoyl chloride[26] over a period of 5 min. After 5 min, 7 mL of water was added to the resulting solution, and after an additional 5 min, another 3 mL of water was added. This resulting mixture was kept stirring in the ice bath for 9 h. The reaction mixture was filtered, and the organic layer was dried over anhydrous magnesium sulfate and concentrated in vacuo to give 1.29 g of the crude product. The crude product was purified by chromatography on a silica gel column with hexanes–ethyl acetate (2:1) to yield 0.33 g of pure *N*-(hex-4-enoyl)-*N*-methylhydroxylamine (20%): TLC (2:1 hexanes–ethyl acetate) R_f 0.25; ^1H NMR ($CDCl_3$, CFT-20) δ 5.40 (m, 2 H), 3.26 (s, 3 H), 2.35 (s, 4 H), 1.63 (m, 3 H); IR (film) 3190 (m), 2930 (m), 1620 (s), 1440 (m), 1390 (m), 1200 (m), 970 (m) cm^{-1}.

Anal. Calcd for $C_7H_{13}NO_2$: C, 58.69; H, 9.14. Found: C, 58.61; H, 8.98.

To a solution containing 1.05 mmol of the *N*-(hex-4-enoyl)-*N*-methylhydroxylamine, prepared above, in 10 mL of carbon tetrachloride was added 1.05 mmol of triethylamine. While the mixture was stirred vigorously, a solution of acetyl chloride (1.06 mmol) in 5 mL of carbon tetrachloride was added dropwise. This reaction mixture was kept at room temperature for 2 h, and 3 mL of water was added. After the separation of the two layers, the aqueous layer was extracted with carbon tetrachloride (2 × 3 mL). All organic portions were combined, dried over anhydrous magnesium sulfate and concentrated in vacuo to yield a yellow oil. Flash column chromatography (silica gel, eluted with 3:1 hexanes–ethyl acetate) of the crude product afforded 0.19 g pure **1a** (96%): TLC (4:1 hexanes–ethyl acetate) R_f 0.26; ^1H NMR ($CDCl_3$, CFT-20) δ 5.40 (m, 2 H), 3.25 (s, 3 H), 2.28 (m, 4 H), 2.20 (s, 3 H), 1.62 (m, 3 H); IR (film) 2940 (m), 1780 (s), 1675 (s), 1430 (m), 1380 (m), 1205 (m), 1165 (s), 1005 (m), 975 (m), 860 (m) cm^{-1}.

Anal. Calcd for $C_9H_{15}NO_3$: C, 58.36; H, 8.10. Found: C, 58.19; H, 8.09.

***N*-(Hex-4-enoyl)-*N*-methyl-*O*-(methoxycarbonyl)-hydroxylamine (1b).** The procedure for the preparation of this compound was the same as the procedure for the preparation of compound **1a**, as described above except that the acylating agent was methyl chloroformate. The yield was 80%: TLC (3:1 hexanes–ethyl acetate) R_f 0.39; ^1H NMR ($CDCl_3$, CFT-20) δ 5.47 (m, 2 H), 3.95 (s, 3 H), 3.32 (s, 3 H), 2.35 (m, 4 H), 1.67 (m, 3 H); IR (film) 2960 (m), 1790 (s), 1675 (s), 1440 (m), 1360 (s), 1275 (m), 935 (m) cm^{-1}.

Anal. Calcd for $C_9H_{15}NO_4$: C, 53.72; H, 7.51. Found: C, 53.53; H, 7.54.

General Procedure for Flash Vacuum Thermolysis. The apparatus that we used for the flash vacuum thermolysis is essentially the same as described previously.[27] The temperature of the reaction tube was controlled by varying the voltage across

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the heating element. The conditions required to induce a reaction were usually determined experimentally. That is, a small sample, just enough for NMR analysis, was evaporated through the tube, and the voltage was adjusted until the yield of the desired product was maximized. The temperature required to induce the reaction was estimated by a thermocouple. Forty volts corresponds to an equilibrium reaction temperature of approximately 515 °C. The temperature of the reaction tube increases by approximately 10°/V. The sample size was usually 20–200 mg.

***N*-Methyl-5-vinyl-2-pyrrolidone (3).** (a) With the general FVT procedure at 60 V, 110 mg of **1a** gave 50 mg of crude products, which contained **3**, 1,5-dimethylpyrrolidone (**5**), and *N*-methyl-3,4-dihydro-2-pyridone (**4**). The mixture was determined by gas chromatography (Se-30, 100 °C) to have a ratio of 40:15:15. Each compound was purified by preparative GC (SE-30, 100 °C). Compound **3**: ^{1}H NMR ($CDCl_3$, NT-300) δ 1.70–1.80 (m, 1 H), 2.19–2.50 (m, 3 H), 2.75 (s, 3 H), 3.88–4.00 (m, 1 H), 5.20–5.30 (m, 2 H), 5.60–5.77 (m, 1 H); IR (film) 2980 (m), 1670 (s), 1430 (m), 1400 (m), 1250 (w) cm^{-1}; MS, *m/z* (relative intensity) 125 (100), 124 (23), 98 (96), 96 (21); high-resolution mass spectrum, *m/z* 125.0841, calcd for $C_7H_{11}NO$ *m/e* 125.0841. The 1,5-dimethyl-2-pyrrolidone was identical with a commercially available sample (Pfaltz and Bauer), and the spectral data for N-methyl-3,4-dihydro-2-pyridone were consistent with those previously reported.[28]

(b) With the general FVT procedure at 55 V, 84 mg of *N*-(hex-4-enoyl)-*O*-(methoxycarbonyl)-*N*-methylhydroxylamine (1b) gave 31.2 mg of ene product **3**. From GLC analysis (SE-30, 100 °C) the desired ene product **3** was 30% pure.

Ethyl [*O*-(Methoxycarbonyl)hydroxamino]acetate (9). A solution of 14.5 g of hydroxylamine hydrochloride in 40 mL of water was cooled in an ice bath and 22.3 g of *tert*-butyl azidoformate added. While the mixture was stirred vigorously, a cold solution of 25.2 g of sodium hydroxide in 85 mL of water was added over 40–50 min, keeping the solution temperature at 5–10 °C. The mixture was allowed to stir in the ice bath for 1 h, and 100 mL of water was added to dissolve the precipitated solid. The solution was extracted twice with 50-mL portions of ether, and the extracts were discarded. The aqueous solution was cooled in an ice bath and acidified to approximately pH 1 with 6 N hydrochloric acid. The resulting mixture was extracted with five 40-mL portions of ether. The combined extracts were dried over anhydrous magnesium sulfate and concentrated in vacuo to give colorless crystals of *N*-*tert*-butoxycarbonyl)hydroxylamine. Recrystallization from 80 mL of petroleum ether–hexanes (5:2) gave 14.3 g (69.5%) colorless crystals, mp 55–56 °C (lit.[29] mp 56–58 °C).

A mixture of 5.35 g of *N*-(*tert*-butoxycarbonyl)hydroxylamine, 3.83 g of methyl chloroformate, and 50 mL of water was stirred well at room temperature while a solution of 3.2 g of sodium hydroxide in 30 mL of water was added during 5–7 min. The solution was allowed to stir in an ice bath for an additional 0.5 h and acidified with 6 N HCl. The resulting mixture was extracted with ether. All organic layers were combined and dried over anhydrous magnesium sulfate. The solvent was removed in vacuo. The resulting thick oil solidified when a seed crystal was added. Recrystallization (hexanes–ether) gave 5.46 g of *N*-(*tert*-butoxycarbonyl)-*O*-(methoxycarbonyl)hydroxylamine as colorless needles (71%), mp 53–54 °C (lit.[30] mp 53–55 °C).

The Standard Alkylation Procedure. *N*-(*tert*-Butoxycarbonyl)-*O*-(methoxycarbonyl)hydroxylamine (2.23 g), potassium carbonate (1.62 g), and ethyl bromoacetate (1.96 g) were mixed with 20 mL of DMF and stirred vigorously at room temperature for 16 h. The mixture was diluted with 70 mL of ether and 30 mL of water. After separation, the organic layer was washed with several portions of water. The resulting organic layer was dried over anhydrous magnesium sulfate and concentrated in vacuo to yield 2.92 g of the crude product. A small portion of this crude product (0.99 g) was purified by chromatography on a silica gel column with a 4:1 hexanes and ethyl acetate mixture as the eluent to afford 0.28 g (28%) of pure *N*-(*tert*-butoxycarbonyl)-*N*-[(ethoxycarbonyl)methyl]-*O*-(methoxycarbonyl)hydroxylamine: ^{1}H NMR ($CDCl_3$, CFT-20) δ 4.20 (m, 4 H), 4.27 (s, 2 H), 4.20 (q, 2 H, J = 7.0 Hz), 3.85 (s, 3 H), 1.50 (s, 9 H), 1.29 (t, 3 H, J = 7.0 Hz); IR (film) 2990 (m), 1795 (s), 1760 (s), 1730 (s), 1445 (m), 1375 (m), 1230 (m), 1160 (m), 1100 (m) cm^{-1}.

Anal. Calcd for $C_{11}H_{19}NO_7$: C, 47.65; H, 6.90. Found: C, 47.78; H, 7.06.

The Standard Hydrolysis Procedure. A solution of 1.49 g of the above hydroxylamine in 5 mL of nitromethane was colled in an ice–acetone bath for 5 min. The cooled solution was treated with a stream of dry HCl for 3–5 min. The resulting solution was kept in the ice bath for an additional 10 min, and the solvent was removed in vacuo. The residue was dissolved in methylene chloride and dried over anhydrous sodium sulfate. The solution was concentrated in vacuo to yield 0.86 g of **9** as a light yellow oil (90%). This compound was used without further purification: ^{1}H NMR ($CDCl_3$, CFT-20) δ 4.20 (q, 2 H, J = 7.0 Hz), 3.80 (s, 3 H), 3.75 (s, 2 H), 1.29 (t, 3 H, J = 7.0 Hz); IR (film) 3260 (m), 3000 (m), 1760 (s), 1445 (m), 1375 (m), 1350 (m), 1270 (s), 1215 (s), 1030 (m), 945 (m), 785 (m) cm^{-1}.

Ethyl [*N*-(Hex-4-enoyl)-*O*-(methoxycarbonyl)hydroxamino]acetate (10). The Standard Acylation Procedure. A solution containing 0.86 g of compound **9** and 0.61 g of sodium carbonate in 10 mL of methylene chloride was cooled. While the mixture was stirred vigorously, a solution of hex-4-enoyl chloride (0.64 g) was added over a period of 5 min. The solution was allowed to stir at room temperature for 24 h. The methylene chloride layer was washed with 10 mL of 5% sodium bicarbonate and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave 0.95 g of the crude product. The crude product was further purified by chromatography on a silica gel column with hexanes–ethyl acetate (3:1) to afford 0.48 g of pure **10** (36%): ^{1}H NMR ($CDCl_3$, CFT-20) δ 5.45 (m, 2 H), 4.40 (s, 2 H), 4.18 (q, 2 H, J = 7.0 Hz), 3.90 (s, 3 H), 2.38 (m, 4 H), 1.65 (m, 3 H), 1.25 (t, 3 H, J = 7.0 Hz); IR (film) 2980 (m), 1795 (s), 1755 (s), 1700 (s), 1440 (m), 1380 (m), 1215 (s) cm^{-1}.

Anal. Calcd for $C_{12}H_{19}NO_6$: C, 52.73; H, 7.00. Found: C, 52.50; H, 6.64.

***N*-[(Ethoxycarbonyl)methyl]-5-vinyl-2-pyrrolidone (12).** With the general FVT procedure at 40 V, 64.8 mg of **10** gave 49.2 mg of **12**. This crude product was further purified by chromatography on a silica gel column using hexanes–ethyl acetate (3:1) to afford 24.7 mg of pure **12** (53%): homogeneous by GC (OV-101, 150 °C); ^{1}H NMR ($CDCl_3$, NT-300) δ 1.28 (t, 3 H, J = 7.0 Hz), 1.74–1.86 (m, 1 H), 2.26–2.48 (m, 3 H), 3.64 (d, 1 H, J = 9.0 Hz), 4.14–4.24 (m, 1 H), 4.18 (q, 3 H, J = 7.0 Hz), 4.32 (d, 1 H, J = 9.0 Hz), 5.21–5.28 (m, 2 H), 5.60–5.71 (m, 1 H); IR (film) 2910 (m), 1740 (s), 1690 (s), 1415 (m), 1260 (m), 1190 (s), 1020 (m) cm^{-1}; MS, *m/z* (relative intensity) 197.2 (M^+, 21.0), 124.2 (100), 110.1 (31.5), 67.1 (21.2); high-resolution mass spectrum, *m/z* 197.1053, calcd for $C_{10}H_{15}NO_3$ *m/z* 197.1053.

***N*-Benzyl-*N*-(hex-4-enoyl)-*O*-(methoxycarbonyl)-hydroxylamine (6).** The standard alkylation procedure using benzyl bromide and *N*-(*tert*-butoxycarbonyl)-*O*-(methoxycarbonyl)hydroxylamine gave 63% of pure *N*-benzyl-*N*-(*tert*-butoxycarbonyl)-*O*-(methoxycarbonyl)hydroxylamine: TLC (4:1 (hexanes–ethyl acetate) R_f 0.48; ^{1}H NMR ($CDCl_3$, CFT-20) δ 7.32 (s, 5 H), 4.78 (s, 2 H), 3.85 (s, 3 H), 1.53 (s, 9 H); IR (film) 2995 (m), 1795 (s), 1735 (s), 1440 (m), 1375 (s), 1265 (s), 1230 (s), 1170 (s), 1110 (m), 935 (m), 710 (m) cm^{-1}.

The standard hydrolysis procedure using the above hydroxylamine gave 99.5% of *N*-benzyl-*O*-(methoxycarbonyl)-hydroxylamine, which was used without further purification: ^{1}H NMR ($CDCl_3$, CFT-20) δ 9.20 (br s, 1 H), 7.38 (s, 5 H), 4.31 (s, 2 H), 3.82 (s, 3 H); IR (film) 3230 (w), 2970 (m), 1800 (s), 1755 (s), 1440 (s), 1270 (s), 760 (m), 710 (s) cm^{-1}.

A solution containing 2.95 mmol of the above hydroxylamine and 2.95 mmol of triethylamine in 10 mL of methylene chloride was cooled in an ice bath. While the mixture was stirred, a solution of hex-4-enoyl chloride (2.95 mmol) in 5 mL of methylene chloride was added dropwise. The resulting mixture was stirred for an additional 2 h in the ice bath. The reaction mixture was washed with 5% sodium bicarbonate (3 × 8 mL), dried over anhydrous magnesium sulfate, and concentrated in vacuo. The crude residue

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was purified by chromatography on a silica gel column with hexanes–ethyl acetate (4:1) to afford 0.50 g of pure **6** (61%): TLC (4:1 hexanes–ethyl acetate) R_f 0.47; ^{1}H NMR ($CDCl_3$, CFT-20) δ 7.30 (s, 5 H), 5.43 (m, 2 H), 4.89 (s, 2 H), 3.85 (s, 3 H), 2.36 (m, 4 H), 1.62 (m, 3 H); IR (film) 1980 (m), 1790 (s), 1685 (s), 1440 (m), 1400 (m), 1250 (s), 1220 (s), 1190 (m), 935 (m), 705 (m) cm^{-1}.

Anal. Calcd for $C_{15}H_{19}NO_4$: C, 64.97; H, 6.91. Found: C, 65.12; H, 6.92.

***N*-Benzyl-5-vinyl-2-pyrrolidone (8).** The general procedure for FVT was used at 40 V. Compound **6** (90 mg) gave rise to a complex crude product (69.6 mg). Flash column chromatography (silica gel, eluted with 20:1 methylene chloride–acetone) of crude product afforded 6.0 mg of pure **8** (9%): TLC (20:1 methylene chloride–acetone) R_f 0.31; ^{1}H NMR ($CDCl_3$, CFT-20) δ 7.23 (s, 5 H), 5.88–5.45 (m, 1 H), 5.25–4.93 (m, 2 H), 4.98 (d, 1 H, J = 16.0 Hz), 3.83 (d, 1 H, J = 16.0 Hz), 3.90 (m, 1 H), 2.58–1.55 (m, 4 H); IR (film) 2945 (m), 1700 (s), 1445 (m), 1265 (m), 721 (m) cm^{-1}; MS, m/z (relative intensity) 201.6 (M$^+$, 62.8), 146.5 (100), 104.4 (59.5), 91.3 (92.8); high-resolution mass spectrum, m/z 201.1150, calcd for $C_{13}H_{15}NO$ m/z 201.1153.

Ethyl [*N*-(Hept-5-enoyl)-*O*-(methoxycarbonyl)hydroxamino]acetate (13). A solution containing 7.26 mmol of *N*-[(ethoxycarbonyl)methyl]-*O*-(methoxycarbonyl)hydroxylamine (**9**) in 10 mL of carbon tetrachloride was cooled in an ice bath; while the mixture was stirred, 7.27 mmol of pyridine was added dropwise. After 5 min, a solution of 7.26 mmol of hept-5-enoyl chloride in 5 mL of carbon tetrachloride was added over a period of 10 min. The mixture was stirred for an additional 2.5 h and then washed with water. The carbon tetrachloride layer was dried over anhydrous magnesium sulfate and concentrated in vacuo. The crude product was further purified by chromatography on silica gel column with hexanes–ethyl acetate (4:1) as eluent to afford pure **13** (54%): TLC (4:1 hexanes–ethyl acetate) R_f 0.39; ^{1}H NMR ($CDCl_3$, CFT-20) δ 5.43 (m, 2 H), 4.45 (s, 2 H), 4.23 (q, 2 H, J = 7.0 Hz), 3.95 (s, 3 H), 2.40 (m, 2 H), 2.15–1.60 (m, 7 H), 1.30 (t, 3 H, J = 7.0 Hz); IR (film) 3000 (m), 1790 (s), 1750 (s), 1690 (s), 1440 (m), 1410 (m), 1380 (m), 1210 (s), 1030 (m) cm^{-1}; MS, m/z (relative intensity) 242.1 (M$^+$ - 45, 0.9), 110.0 (31.9), 83.1 (92.6), 68.0 (29.4), 55.1 (100).

Anal. Calcd for $C_{13}H_{21}NO_6$: C, 54.35; H, 7.37. Found: C, 54.51; H, 7.21.

***N*-[(Ethoxycarbonyl)methyl]-6-vinyl-2-piperidone (15).** With the general FVT procedure at 40 V, 213 mg of **13** gave the crude product, which was purified on silica gel column with hexanes–ethyl acetate (1:1) as eluent to afford 15.8 mg of ene product (6.7%): TLC (1:1 hexanes–ethyl acetate) R_f 0.60; ^{1}H NMR ($CDCl_3$, CFT-20) δ 5.95–5.55 (m, 1 H), 5.25–4.98 (m, 2 H), 4.46 (d, 1 H, J = 17.5 Hz), 4.10 (q, 2 H, J = 7.5 Hz), 3.59 (d, 1 H, J = 17.5 Hz), 2.44 (m, 1 H); IR (film) 2970 (s), 2890 (s), 1745 (s), 1645 (s), 1460 (s), 1405 (m), 1375 (m), 1275 (m), 1200 (s), 1140 (m), 1040 (s), 1000 (m) cm^{-1}; MS, m/z (relative intensity) 211.0 (M$^+$, 1.8), 182.0 (0.6), 55.0 (100), 42.0 (47.2), 41.0 (66.0), 29.1 (51.9); high-resolution mass spectrum, m/z 211.1206, calcd for $C_{11}H_{17}NO_3$ m/z 211.1209.

***N*-Ethyl-*N*-(hex-4-enoyl)-*O*-(methoxycarbonyl)hydroxylamine (16).** The standard alkylation procedure using *N*-(*tert*-butoxycarbonyl)-*O*-(methoxycarbonyl)hydroxylamine and ethyl iodide followed by flash column chromatography (silica gel, with 3:1 hexanes–ethyl acetate as eluent) gave *N*-ethyl-*N*-(*tert*-butoxycarbonyl)-*O*-(methoxycarbonyl)hydroxylamine as a colorless oil in 84% yield, homogeneous by TLC (3:1 hexanes–ethyl acetate), R_f 0.51: ^{1}H NMR ($CDCl_3$, CFT-20) δ 3.85 (s, 3 H), 3.60 (q, 2 H, J = 7.0 Hz), 1.97 (s, 9 H), 1.19 (t, 3 H, J = 7.0 Hz); IR (film) 3010 (m), 1790 (s), 1720 (s), 1440 (m), 1370 (s), 1240 (s), 1140 (s), 1080 (m), 930 (m), 850 (m), 760 (m) cm^{-1}.

The standard hydrolysis procedure using the above hydroxylamine afforded 82% of *N*-ethyl-*O*-(methoxycarbonyl)-hydroxylamine, which was used without further purification: ^{1}H NMR ($CDCl_3$, CFT-20) δ 6.75 (t, 1 H, J = 7.0 Hz), 3.81 (s, 3 H), 3.10 (q', 2 H, J = 7.0 Hz), 1.17 (t, 3 H, J = 7.0 Hz); IR (film) 3300 (m), 3015 (s), 1750 (s), 1445 (s), 1385 (m), 1250 (s), 1125 (s), 930 (m) cm^{-1}.

Using the standard acylation procedure with the above hydroxylamine and hex-4-enoyl chloride gave **16**. Purification by flash column chromatography on silica gel (hexanes–ethyl acetate (5:1)) gave pure **16** as a colorless oil in 70% yield: TLC (5:1 hexanes–ethyl acetate) R_f 0.51; ^{1}H NMR ($CDCl_3$, CFT-20) δ 5.55–5.30 (m, 2 H), 3.93 (s, 3 H), 3.77 (q, 3 H, J = 7.0 Hz), 2.50–2.00 (m, 4 H), 1.70–1.45 (m, 3 H), 1.19 (t, 3 H, J = 7.0 Hz); IR (film) 2970 (m), 2950 (m), 1790 (s), 1680 (s), 1445 (m), 1410 (m), 1350 (w), 1245 (s), 1160 (m), 975 (m), 935 (m), 785 (m) cm^{-1}.

Anal. Calcd for $C_{10}H_{17}NO_4$: C, 55.80; H, 7.96. Found: C, 55.47; H, 8.17.

***N*-(Hex-4-enoyl)-*N*-vinylamine (19).** With the general procedure for FVT at 65 V, 201.3 mg of **16** gave 71.5 mg of crude product, which was purified by flash column chromatography (silica gel, eluted with 4:1 hexanes–ethyl acetate) to afford 6% of pure **19**, homogeneous by GC (SE-30); TLC (4:1 hexanes–ethyl acetate) R_f 0.32; ^{1}H NMR ($CDCl_3$, CFT-20) δ 7.70–6.60 (br s, 1 H), 7.13–6.70 (m, 1 H), 5.75–5.15 (m, 2 H), 4.53 (d, 1 H, J = 20.0 Hz), 4.38 (d, 1 H, J = 12.0 Hz), 2.25 (br s, 4 H), 1.95–1.55 (m, 3 H); IR (film) 3295 (m), 2940 (m), 1670 (s), 1640 (s), 1545 (m), 1400 (m), 1240 (m), 990 (m), 975 (m), 860 (m) cm^{-1}; MS, m/z (relative intensity) 139 (M$^+$, 4.1), 110.1 (85.2), 69.1 (100), 55.1 (89.6), 43.1 (74.7); high-resolution mass spectrum, m/z 139.1002, calcd for $C_8H_{13}NO$ m/z 139.0998.

***N*,*O*-Bis(methoxycarbonyl)-*N*-(hept-2-en-7-yl)-hydroxylamine (20).** The standard alkylation procedure using *N*,*O*-bis(methoxycarbonyl)hydroxylamine and 1-bromo-5-heptene followed by flash column chromatography (silica gel, with 5:1 hexanes–ethyl acetate as eluent) gave **20** as a colorless oil in 60% yield, which was homogeneous by TLC (5:1(hexanes–ethyl acetate) R_f 0.41: ^{1}H NMR ($CDCl_3$, CFT-20) δ 5.50–5.30 (m, 2 H), 3.90 (s, 3 H), 3.78 (s, 3 H), 3.63 (t, 2 H, J = 7.0 Hz), 2.15–1.15 (m, 9 H); IR (film) 2975 (m), 1790 (s), 1720 (s), 1440 (s), 1240 (s), 1180 (s) cm^{-1}.

Anal. Calcd for $C_{11}H_{19}NO_5$: C, 53.87; H, 7.81. Found: C, 53.44; H, 7.72.

(1*E*,5*E*)-1-[*N*-(Methoxycarbonyl)amino]-1,5-heptadiene (22a) and (1*Z*,5*E*)-1-[*N*-(Methoxycarbonyl)amino]-1,5-heptadiene (22b). Thermolysis of compound **20** was performed by following the general FVT procedure at 40 V. The reaction mixture was separated on preparative gas chromatography (OV-17, 130 °C) to give compound **22a** and **22b**. These two compounds were further purified by chromtography on a silica gel column with hexanes–ethyl acetate (6:1) as eluent to afford pure **22a** and **22b**.

Compound 22a. The isolation yield of this compound was 16%. It was shown by GC to be 96% pure and homogeneous by TLC (1:1 hexanes–ethyl acetate), R_f 0.31: ^{1}H NMR ($CDCl_3$, NT-300) δ 6.46 (t, 1 H, J = 12.0 Hz), 6.33 (s, 1 H), 5.52–5.39 (m, 2 H), 5.08–4.92 (m, 1 H), 3.71 (s, 3 H), 2.19–1.92 (m, 4 H), 1.70–1.57 (m, 3 H); IR (CCl_4) 3475 (m), 2950 (m), 1740 (s), 1680 (m), 1500 (s), 1450 (m), 1220 (s), 1050 (m), 970 (m), 950 (m) cm^{-1}; MS, m/z (relative intensity) 169.0 (M$^+$, 4.9), 82.0 (11.1); high-resolution mass spectrum, m/z 169.1101, calcd for $C_9H_{15}NO_2$ m/z 169.1103.

Compound 22b. The isolation yield of compound was 21%. It was judged by GC to have greater than 96% purity, and was homogeneous by TLC (1:1 hexanes–ethyl acetate), R_F 0.36: ^{1}H NMR ($CDCl_3$, NT-300) δ 6.44 (t, 1 H, J = 8.0 Hz), 6.32 (s, 1 H), 5.55–5.35 (m, 2 H), 4.63 (q, 2 H, J = 8.0 Hz), 3.73 (s, 3 H), 2.20–1.94 (m, 4 H), 1.70–1.61 (m, 3 H); IR (CCl_4) 3475 (m), 2950 (m), 1740 (s), 1670 (m), 1540 (m), 1490 (m), 1450 (m), 1350 (m), 1215 (s), 1080 (m), 1000 (m), 970 (m) cm^{-1}; MS, m/z (relative intensity) 169.2 (M$^+$, 4.8), 114.1 (100), 82.1 (16.9), 59.1 (6.4); high-resolution mass spectrum, m/z 169.1104, calcd for $C_9H_{15}NO_2$ m/z 169.1103.

Ethyl 2-[*N*-Acetyl-*O*-(methoxycarbonyl)hydroxamino]-butyrate (23). The standard alkylation procedure was followed using ethyl 2-bromobutyrate and *N*-(*tert*-butoxycarbonyl)-*N*-(methoxycarbonyl)hydroxylamine to afford 50% of pure ethyl 2-[*N*-(*tert*-butoxycarbonyl)-*O*-(methoxycarbonyl)hydroxamino]-butyrate: TLC (4:1 hexanes–ethyl acetate) R_f 0.41; ^{1}H NMR ($CDCl_3$, CFT-20) δ 4.58 (dd, 1 H, J = 7.4 Hz, J = 5.0 Hz), 4.20 (q, 3 H, J = 7.0 hz), 3.38 (s, 3 H), 1.50 (s, 9 H), 1.27 (t, 3 H, J = 7.0 Hz), 1.06 (t, 3 H, J = 7.4 Hz); IR (film) 2990 (m), 1795 (s), 1740 (s), 1440 (m), 1370 (s), 1320 (m), 1240 (s), 1170 (m), 1135 (m), 1030 (m), 945 (w), 860 (w), 780 (w) cm^{-1}.

Anal. Calcd for $C_{13}H_{23}NO_7$: C, 51.14; H, 7.59. Found: C, 51.83; H, 7.62.

The standard hydroylsis procedure using the above hydroxylamine afforded 90% of ethyl 2-[O-(methoxycarbonyl)hydroxamino]butyrate: ^{1}H NMR ($CDCl_3$, CFT-20) δ 4.20 (q, 2 H, J =

7.0 Hz), 3.80 (s, 3 H), 3.71 (t, 1 H, J = 7.0 Hz), 1.70 (q, 2 H, J = 7.0 Hz), 1.30 (t, 3 H, J = 7.0 Hz), 1.03 (t, 3 H, J = 7.0 Hz); IR (film) 3260 (w), 2990 (m), 1760 (s), 1735 (s), 1445 (m), 1375 (w), 1260 (s), 1210 (s), 1100 (w), 1025 (m), 940 (w), 870 (w), 785 (m) cm^{-1}.

The standard acylation procedure was followed using the above hydroxylamine and acetyl chloride to give crude **23**. The residue was purified by chromatography on Chromatotron (1-mm plate) using hexanes–ethyl acetate (4:1) as eluent to give 42% of pure **23**: ^1H NMR ($CDCl_3$, CFT-20) δ 4.91 (d, d, 1 H, J = 5.7 Hz, J = 5.0 Hz), 4.15 (q, 2 H, J = 7.5 Hz), 3.90 (s, 3 H), 2.13 (s, 3 H), 2.10–1.65 (br m, 2 H), 1.25 (t, 3 H, J = 7.5 Hz), 1.00 (t, 3 H, J = 7.0 Hz); IR (film) 2965 (m), 1790 (s), 1730 (s), 1435 (s), 1310 (s), 1230 (s), 1130 (m), 1080 (m), 1020 (m), 930 (m) cm^{-1}.

Anal. Calcd for $C_{10}H_{17}NO_6$: C, 48.58; H, 6.93. Found: C, 48.29; H, 6.93.

(*Z*)- and (*E*)-Ethyl 2-(acetylamino)crotonates (24 and 25). With the general FVP procedure at 35 V, 137.3 mg of **23** gave 91 mg of **24** and **25**. This mixture was purified by chromatography on Chromatotron (1-mm plate) using hexanes–ethyl acetate (5:2, then to 5:3) to give 29.2 mg (31%) of the E isomer: TLC (5:2 hexanes–ethyl acetate) R_f 0.17; ^1H NMR ($CDCl_3$, NT-300) δ 7.37 (br s, 1 H), 7.21 (q, 1 H, J = 7.2 Hz), 4.29 (q, 2 H, J = 7.2 Hz), 2.07 (s, 3 H), 2.07 (d, 3 H, J = 7.2 Hz), 1.34 (t, 3 H, J = 7.2 Hz).

Further elution gave 55.5 mg (59%) of the Z isomer: TLC (5:2 (hexanes–ethyl acetate) R_f 0.07; ^1H NMR ($CDCl_3$, NT-300) δ 6.80 (q, 1 H, J = 7.2 Hz), 6.80 (br s, 1 H), 4.21 (q, 2 H, J = 7.2 Hz), 2.12 (s, 3 H), 1.77 (d, 3 H, J = 7.2 Hz), 1.28 (t, 3 H, J = 7.2 Hz). The data on these compounds are consistent with those previously reported in the literature.[20]

Ethyl [*N*-(Cyclopent-2-en-1-ylacetyl)-*O*-(methoxycarbonyl)hydroxamino]acetate (26). To a solution containing 4.32 mmol of **9** in 20 mL of carbon tetrachloride cooled, while stirring, in an ice bath, was added a solution of triethylamine (4.32 mmol) in 5 mL of carbon tetrachloride. To this reaction mixture was added a solution of cyclopent-2-enylacetyl chloride (4.76 mmol in 10 mL of carbon tetrachloride). The resulting solution was stirred in an ice bath for an additional 3 h, and then 20 mL of water was added. The organic layer was separated, washed with 5% sodium bicarbonate (2 × 10 mL), and dried over anhydrous magnesium sulfate. This solution was concentrated in vacuo to afford a complex mixture. This crude mixture was purified by chromatography on a silica gel column with hexanes–ethyl acetate (4:1) as eluent to give 0.42 g of pure **26** (34%): TLC (4:1 hexanes–ethyl acetate) R_f 0.40; ^1H NMR ($CDCl_3$, NT-300) δ 5.76 (m, 1 H), 5.72 (m, 1 H), 4.47 (s, 2 H), 4.21 (q, 2 H, J =v 7.0 Hz), 3.93 (s, 3 H), 3.16 (t, 1 H, J = 8.0 Hz), 2.54–2.09 (m, 5 H), 1.53–1.40 (m, 1 H), 1.27 (t, 3 H, J = 7.0 Hz); IR (film) 2975 (m), 1795 (s), 1755 (s), 1690 (s), 1440 (m), 1375 (m), 1230 (m), 1270 (s), 1250 (m), 1210 (m), 1045 (m), 935 (m) cm^{-1}.

Anal. Calcd for $C_{13}H_{19}NO_6$: C, 54.73; H, 6.71. Found: C, 54.43; H, 6.73.

Ethyl 1-[*N*-(Cyclopent-2-en-1-ylacetyl)amino]-1-methoxyacetate (29). With the general FVT procedure at 35 V, 153.8 mg of **26** gave a complex mixture. Flash column chromatography (silica gel, eluted with 2:1 hexanes–ethyl acetate) of the crude residue afforded a colorless oil (20 mg, 15%), homogeneous by TLC, R_f 0.21: ^1H NMR ($CDCl_3$, CFT-20) δ 6.84–6.34 (br s, 1 H), 6.03–5.68 (m, 2 H), 5.58 (d, 1 H, J = 8.0 Hz), 4.36 (t, 2 H, J = 7.0 Hz), 3.60 (s, 3 H), 3.38–3.57 (m, 1 H), 2.63–2.08 (m, 5 H), 1.86–1.31 (m, 1 H), 1.49 (t, 3 H, J = 7.0 Hz); IR (film) 3340 (m), 2950 (m), 1750 (s), 1665 (s), 1525 (s), 1380 (m), 1200 (s), 1100 (s), 1040 (m) cm^{-1}; MS, m/z (relative intensity) 209.1 (M^+ – 32, 74.4), 80.1 (88.6), 67.1 (80.3), 60.1 (100); high-resolution mass spectrum, m/z 209.1052, calcd for $C_{11}H_{15}NO_3$ m/z 209.1051.

Ethyl [*N*-((4*Z*)-5-(Ethoxycarbonyl)hex-4-enoyl)-*O*-(methoxycarbonyl)hydroxamino]acetate carbonyl)hydroxamino]acetate (30). Triethylamine (4.03 mmol) was added dropwise to a solution containing 4.03 mmol of **9** in 15 mL of carbon tetrachloride cooled in an ice bath, while being stirred. After 5 min, a solution of (4*Z*)-5-(ethoxycarbonyl)hex-4-enoyl chloride,[31] prepared from the acid with thionyl chloride in 10 mL of carbon tetrachloride, was added dropwise. This resulting solution was stirred for an additional 1 h, and then 15 mL of water was added. The two layers were separated. The organic layer was further washed with 5% sodium bicarbonate (2 × 10 mL) and water (2 × 10 mL) and then dried over anhydrous magnesium sulfate. This solution was concentrated in vacuo to yield 1.39 g of crude product. This crude product was purified by chromatography on silica gel column with hexanes–ethyl acetate (2:1) as eluent to afford 0.54 g of pure **30** (39%): TLC (2:1 hexanes–ethyl acetate) R_f 0.35; ^1H NMR ($CDCl_3$, CFT-20) δ 5.96 (m, 1 H), 4.44 (s, 2 H), 4.19 (q, 3 H, J = 7.0 Hz), 4.13 (q, 3 H, J = 7.0 Hz), 3.93 (s, 3 H), 3.00–2.40 (m, 4 H), 1.87 (m, 3 H), 1.30 (t, 3 H, J = 7.0 Hz), 1.28 (t, 3 H, J = 7.0 Hz); IR (film) 2910 (m,) 1790 (s), 1745 (s), 1705 (s), 1440 (m), 1370 (m), 1200 (s), 1120 (m), 930 (m), 770 (m) cm^{-1}.

Anal. Calcd for $C_{15}H_{23}NO_8$: C, 52.17; H, 6.71. Found: C, 52.34; H, 6.94.

Ethyl [*N*-((4*E*)-5-(Ethoxycarbonyl)hex-4-enoyl)-*O*-(methoxycarbonyl)hydroxamino]acetate (33). The procedure for the preparation of this compound was the same as the procedure for the preparation of compound **30**, as described above, except that the E isomer[31] was used and the reaction time was 3 h. The crude product was purified by chromatography on silica gel column with hexanes–ethyl acetate (3:1) as eluent to afford pure **33** (45%): TLC (2:1 hexanes–ethyl acetate) R_f 0.30; ^1H NMR ($CDCl_3$, CFT-20) μ 6.75 (m, 1 H), 4.44 (s, 2 H), 4.19 (q, 2 H, J = 7.0 Hz), 4.15 (q, 2 H, J = 7.0 Hz), 2.25 (m, 4 H), 1.85 (s, 3 H), 1.28 (t, 3 H, J = 7.0 Hz), 1.27 (t, 3 H, J = 7.0 Hz); IR (film) 3010 (m), 1790 (s), 1750 (s), 1700 (s), 1440 (m), 1415 (m), 1365 (m), 1270 (s), 1200 (s), 1115 (m), 1020 (m), 930 (m) cm^{-1}.

Anal. Calcd for $C_{15}H_{23}NO_8$: C, 52.17; H, 6.71. Found: C, 51.80; H, 6.83.

***N*-[(Ethoxycarbonyl)methyl]-5-[1-(ethoxycarbonyl)-vinyl]-2-pyrrolidone (32).** (a) With the general FVT procedure at 35 V, 37.1 Mg of compound **30** gave 29.4 mg of the crude product. This crude product was purified by flash column chromatography using hexanes–ethyl acetate (1:1) as eluent to afford 15 mg (52%) of ene adduct **32**: TLC (1:1 hexanes–ethyl acetate) R_f 0.26; ^1H NMR ($CDCl_3$, NT-300) δ 6.34 (s, 1 H), 5.61 (s, 1 H), 4.69 (m, 1 H), 4.54 (d, 1 H, J = 7.0 Hz), 4.30–4.17 (m, 4 H), 3.43 (d, 1 H, J = 7.0 Hz), 2.60–2.39 (m, 3 H), 1.96–1.81 (m, 1 H), 1.32 (t, 3 H, J = 7.0 Hz), 1.27 (t, 3 H, J = 7.0 Hz); IR (film) 3005 (m), 2945 (m), 1755 (s), 1715 (s), 1640 (w), 1450 (m), 1430 (m), 1385 (m), 1310 (m), 1275 (m), 1210 (s), 1040 (m), 980 (w) cm^{-1}; MS, m/z (relative intensity) 269.1 (M^+, 5.9), 196.0 (100), 195.0 (62), 166.0 (43.1), 150.0 (65.8); high-resolution mass spectrum, m/z 269.1258; calcd for $C_{13}H_{19}NO_5$ m/z 269.1263.

(b) With the same conditions as above, 31.0 mg of compound **33** gave 17.4 mg of the crude product. TLC analysis and the NMR spectrum of this crude product indicated it was a complex mixture, and it was not further purified. The ^1H NMR spectrum (NT-300) of the product indicated that the ene adduct **32** was approximately 24% of the mixture.

2,5-Dihydro-4-methyl-5-oxo-2-furanacetyl Chloride (37). To a solution containing 17.3 mmol of 2,5-dihydro-4-methyl-5-oxo-2-furanacetic acid[32] in 10 mL of dry benzene was added 6 mL of thionyl chloride. This reaction mixture was refluxed for 2 h and then stirred at room temperature for an additional 12 h. The solvent and the excess thionyl chloride were removed in vacuo. The residue was purified by a bulb-to-bulb distillation to afford 13.3 mmol of compound **37** as light yellow oil: ^1H NMR ($CDCl_3$, CFT-20) δ 7.10 (t, 1 H, J = 1.6 Hz), 5.29 (tt, 1 H, J = 7.5 Hz, J = 1.6 Hz), 3.31 (d, 1 H, J = 2.4 Hz), 3.22 (d, 1 H, J = 2.2 Hz), 1.95 (t, 3 H, J = 1.9 Hz), IR (film) 2935 (m), 1795 (s), 1755 (s), 1655 (m), 1395 (m), 1375 (m), 1340 (m), 1215 (m), 1105 (m), 1070 (s), 1005 (m), 870 (m), 760 (m), 700 (m) cm^{-1}.

Ethyl [*N*-((2,5-Dihydro-4-methyl-5-oxo-2-furyl)acetyl)-*O*-(methoxycarbonyl)hydroxamino]acetate (38). The standard acylation procedure was followed using **9** and **37**. The crude mixture (430 mg) was chromatographed on silica gel column with hexanes–ethyl acetate (1:1) as eluent to give 170 mg of compound **38** (18.4%): TLC (1:1 hexanes–ethyl acetate) R_f 0.32; ^1H NMR ($CDCl_3$, NT-300) δ 5.35–5.25 (m, 1 H), 4.53 (d, 1 H, J = 16.0 Hz), 4.42 (d, 1 H, J = 16.0 Hz), 4.23 (q, 2 H, J = 7.0 Hz),

(31) Kossanyi, J.; Perales, J.; Lachach, A.; Kawenoki, I.; Morizur, J. P. *Synthesis* **1979**, 279.

(32) The acid chloride was prepared from the known acid: Scharf, H.-D.; Mattay, J. *Liebigs Ann. Chem.* **1977**, 770.

3.96 (s, 3 H), 3.13 (dd, 1 H, J = 8.0 Hz, J = 6.0 Hz), 2.57 (dd, 1 H, J = 8.0 Hz, J = 8.0 Hz), 1.97 (t, 3 H, J = 2.0 Hz), 1.30 (t, 3 H, J = 7.0 Hz); IR (film) 2980 (m), 1800 (s), 1765 (s), 1690 (s), 1445 (m), 1380 (m), 1255 (s), 1220 (s), 1105 (m), 1045 (m), 740 (m) cm^{-1}; MS, m/z (relative intensity) 270.1 (M^+ - 45, 1.3) 139.1 (43.1), 125.1 (33.0), 111.1 (1.8), 97.1 (100); high-resolution mass spectrum, m/z 270.0611, calcd for $C_{11}H_{12}NO_7$ m/z 270.0613.

Pyrrolidinone 40. With the general FVT procedure at 35 V, 89.1 mg of compound **38** gave 55.1 mg of the crude product **40**. This crude product was chromatographed on silica gel (1:3 hexanes-ethyl acetate) to afford 22.1 mg of pure **40** (32.6%): TLC (1:3 hexanes-ethyl acetate) R_f 0.22; ^1H NMR ($CDCl_3$, NT-300) δ 6.49 (d, 1 H, J = 1.0 Hz), 5.92 (d, 1 H, J = 1.0 Hz), 5.11 (td, 1 H, J = 6.0 Hz, J = 1.0 Hz), 4.96 (d, 1 H, J = 3.0 Hz), 4.48 (d, 1 H, J = 18.0 Hz), 4.27-4.15 (m, 2 H), 3.60 (d, 1 H, 3.60 (d, 1 H, J = 18.0 Hz), 2.97-2.78 (7, 2 H), 1.29 (t, 3 H, J = 7.2 Hz); IR (CH_2Cl_2) 2940 (m), 1775 (s), 1745 (s), 1715 (s), 1430 (m), 1410 (m), 1380 (m), 1220 (s), 1130 (m), 1045 (m) cm^{-1}; MS, m/z (relative intensity) 239.1 (M^+, 8.3), 197.1 (25.0), 167.1 (10.1), 166.0 (100), 138.1 (14.1); high-resolution mass spectrum, m/z 239.0793, calcd for $C_{11}H_{13}NO_5$ m/z 239.0794.

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Effects of Halogen Substitution on Reactions of *o*-Quinol Acetates with Isopropylmagnesium Bromide and Diisopropylmagnesium. Competition between Unimolecular Decomposition and Bimolecular Reactions of Radical Anions

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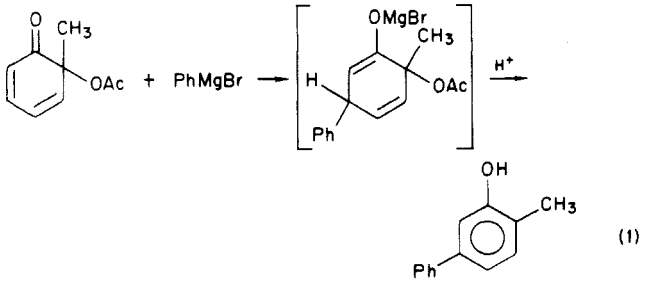
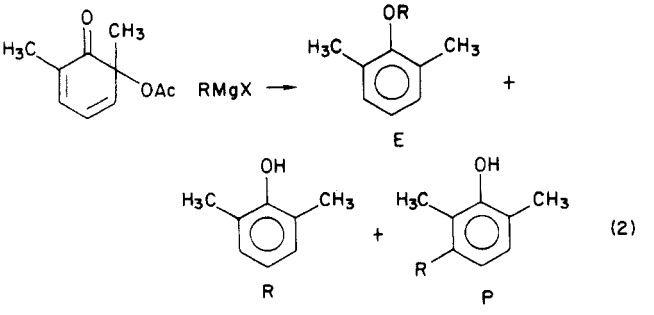
When a single methyl substituent at C-2 or C-4 of an *o*-quinol acetate (1) is replaced by a halogen atom, a greatly decreased yield of the corresponding 3-isopropylphenol is obtained from reaction of 1 with isopropylmagnesium bromide. Replacement of a second methyl group by halogen results in a marked *increase* in the yield of the 3-isopropylphenol. Essentially identical product distributions are obtained from reactions of halogenated *o*-quinol acetates with concentrated and dilute Grignard solutions and with diisopropylmagnesium, in contrast to reactions with halogen-free *o*-quinol acetates. Reactions with hexadeuterioisopropylmagnesium bromide gave reduction products bearing increasing percentages of deuterium at C-3 as the number of bromines on the rings of the ω-quinol acetates increased. These data are consistent with reactions of halogenated *o*-quinol acetates, in contrast to those of halogen-free analogues, proceeding solely by SET processes. The reactions of halogen-stabilized radical anions with isopropyl radicals compete with decomposition of the radical anions to phenoxy radicals.

Three decades ago, F. Wessely and his co-workers at the University of Vienna reported that alkyl or aryl groups can be introduced at positions meta to the hydroxy groups of phenols by reacting *o*-quinol acetates (6-acetoxy-2,4-cyclohexa-2,4-dien-1-ones) with Grignard reagents (e.g., eq. 1).[1]



(1)

Our research group later demonstrated that the synthetic utility of this process is largely limited to the introduction of aryl or primary alkyl groups. The reactions of *o*-quinol acetates with secondary or tertiary Grignard reagents,[2] or with benzylic Grignards,[2,3] yielded alkyl aryl ethers E and reduction products (the parent phenols R) as the principal products. *m*-Alkylphenols P were obtained in significant yields when secondary alkyl Grignards were employed but were only trace products from reactions of *o*-quinol acetates with tertiary or benzylic Grignards. Products resulting from 1,2-addition to the carbonyl groups were obtained in significant yields from reactions with



(2)

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