Generation of Aldehydic Enol Ethers and Enamines by Olefination of Ketones[1]

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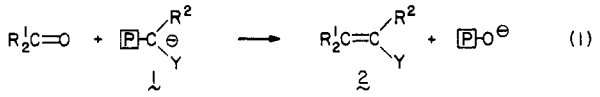
Reaction of aliphatic ketones with dimethyl (diazomethyl)phosphonate (**5**, R = CH_3) in the presence of alcohols and amines afforded enol ethers and enamines, respectively, of the next higher aldehyde. The technique has been found to be applicable to several sterically hindered ketones, among which was camphor. Although conjugated ketones did not yield the desired aldehyde derivative, β,γ-unsaturated ketones did so without complications caused by competing conjugation of the carbon–carbon double bond.

There is considerable interest in synthetic methodologies that result in elaboration of aldehydes and ketones into the *O*-alkyl enol ethers[2] and the enamines[3] of the next higher carbonyl compounds. Pre-eminent among the routes for accomplishing this transformation are the Wittig olefination reaction and modifications thereof,[4] which involve use of a phosphorus-containing species, **1**, as a nucleophile (eq 1).

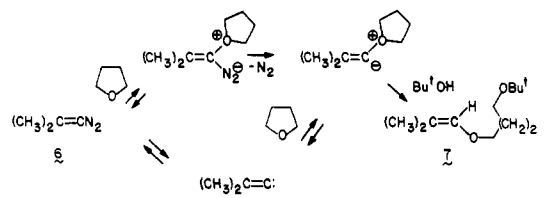


(1)

a. P = $Ph_3P^{\oplus}$, Y = OR [5]
b. P = $Ph_2P(O)$, Y = OR [7]
c. P = $(RO)_2P(O)$, Y = OR [6]
d. P = $(R_2N)_2P(O)$, Y = OR [5h]
e. P = Ph_2P, Y = OR [8]
f. P = $Ph_2P(O)$, Y = Morpholino [9m]
g. P = $(RO)_2P(O)$, Y = NR_2 [9a-d,f-h]
h. P = $(RO)_2P(O)$, Y = N=CHPh [9ikl]
i. P = $Ph_2P(O)$, Y = N=CPh_2 [9j]
j. P = $(RO)_2P(O)$, Y = $\overset{\oplus}{N}\equiv\overset{\ominus}{C}$ [9e]

Several reagents, examples of which include **1a–e**,[5] have been developed for use in preparation of the enol ethers, and problems associated with the use of some of them have been noted. Specifically, the phosphoranes **1a**[5] are unstable[5d] and may give low yields in the reaction,[5a,h,j] whereas use of the phosphonates **1b,c**[6] and the phosphine oxides **1d**[7] requires either extended heating of the salts formed initially or counterion exchange for completion of the reaction. Strong bases, e.g., LDA and *sec*-butyllithium, are needed for efficient generation of anions **1a–e**, and all of them, save for **1e**,[8] appear to promote enolization in preference to nucleophilic attack with sterically hindered substrates. Moreover, if it is of interest to make a series of enol ethers in which the nature of the *O*-alkyl group is varied, a separate phosphorus-containing reagent, **1** (Y = OR), must be prepared for each member of the series.

Scheme I

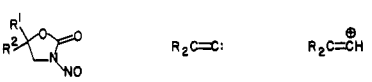


Similar problems attend the use of the reagents **1f–h**[9] for the preparation of enamines in that strong bases are needed to generate these nucleophiles, heating or cation exchange is required for elimination of the initially formed 1,2-adduct to produce the enamine, and enolization of substrates can be a problem. Once again, variation of the nature of the substituents at nitrogen necessitates synthesis of separate aminomethyl reagents, **1** (Y = NR_2).

The present paper describes an alternate method for olefination of ketones to aldehydic enol ethers and enamines. Importantly, some of the shortcomings associated with the use of the reagents **1** for this type of transformation have been overcome.

Results and Discussion

Development of the present method was based on two types of observations. First, it had been reported by Newman et al. that base-promoted decomposition of *N*-nitrosooxazolidones **2** in alcoholic media afforded enol



2 **3** **4**

(1) Preliminary account of this work: Gilbert, J. C.; Weerasooriya, U. *Tetrahedron Lett.* **1980**, *21*, 2041.

(2) A succinct description of the chemistry of these substances can be found in: Earnshaw, C.; Wallis, C. J.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1979**, 3099.

(3) Reviews of enamine chemistry: Cook, A. G., Ed. (a) "Enamines: Synthesis, Structure, and Reactions"; Marcel Dekker: New York, 1969. (b) Kuehne, M. E. *Synthesis* **1970**, 510. (c) Hickmott, P. W. *Tetrahedron* **1982**, *38*, 1975.

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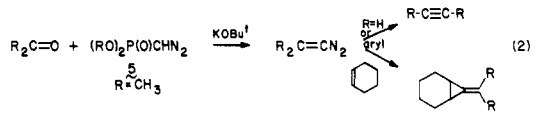
Table I. Saturated Enol Ethers[a]

entry	substrate	solvent	product[b]	% yield[c]
1	cyclohexanone	CH_3OH	8a	53
2[d]	cyclohexanone	CH_3OH	8a	58
3[e]	cyclohexanone	CH_3OH	8a	70
4[f]	cyclohexanone	CH_3OH	8a	65
5	cyclohexanone	CH_2CH_2OH	8b	73
6	cyclohexanone	$(CH_3)_2CHOH$	8c	71
7[g]	cyclohexanone	$(CH_3)_2CHOH$	8c	71
8	cyclohexanone	$(CH_3)_3COH$	8d	56
9	cyclopentanone	CH_3OH	9a	30
10[d]	cyclopentanone	CH_3OH	9a	33
11[h]	cyclopentanone	CH_3OH	9a	29
12	cyclooctanone	CH_3OH	10a	0
13	adamantanone	$(CH_3)_3COH$	11	74
14[f]	2-methylcyclohexanone	CH_3OH	12a	45
			12b	16
15	2,4,4-trimethylcyclohexanone	CH_3OH	12c	41
			12d	4
16	*endo*-1,4,4a,4b,7,8a-hexahydro-1,4-methanonaphthalene-5,8-dione	CH_3OH	13a	42[i]
			13b	12[i]
17	3,5,5-trimethyl-2-cyclohexen-1-one	CH_3OH	14a	0
18[f]	4-methyl-3-cyclohexen-1-one	CH_3OH	15a	56
19	camphor	CH_3OH	16a	0[j]
20[d]	5-nonanone	CH_3OH	17a	20
21[d]	3,3-dimethyl-2-butanone	CH_3OH	18a	36
22	4-nitrobenzaldehyde	CH_3OH	19a	80[k]
23	2-phenylethanal	CH_3OH	19b	69[k]
24	acetophenone	CH_3OH	19c	20[k]
25	4-nitroacetophenone	CH_3OH	19d	55[k]
			20a	16
			20b	16
26[d]	cyclohexanone/4-nitrobenzaldehyde (1:1 molar ratio)	CH_3OH	19a	70
			8a	0
27[l]	cyclohexanone/4-nitrobenzaldehyde (1:1 molar ratio)	CH_3OH	19a	77
			8a	19

[a] The "General Procedure for Enol Ethers" (see Experimental Section) was followed unless otherwise noted. [b] See Chart I. [c] Yields were determined by integration of ^1H NMR spectra and have not been optimized. [d] Reagents were stirred at −78 °C for 10–24 h and at 25 °C for 2–24 h prior to the workup. [e] The phosphonate **5** was used in a ratio of 2.2:1.0 relative to ketone. [f] Potassium carbonate was used as the base. [g] Lithium hydroxide was used as the base. [h] Reagents were stirred at −100 °C for 1 h, at −78 °C for 10 h, and at 25 °C for 24 h. [i] Isolated yield. [j] Camphor recovered in 94% yield. [k] See ref 12c for the experimental procedure. [l] 4-Nitrobenzaldehyde added after other reactants had been combined and stirred for 10 h at −78 °C.

ethers in good yields.[10] They implicated alkylidenecarbenes **3** as likely intermediates in the reaction, although vinyl cations **4** were also considered as possible precursors. Second, we had observed that base-promoted reaction of dimethyl (diazomethyl)phosphonate (**5**)[11] with aldehydes and ketones apparently produced alkylidenecarbenes, on the basis of the nature of the products obtained (eq 2).[12]



Moreover, the enol ether **7** was formed in 15% yield during attempts to generate 1-diazo-2-methyl-1-propene (**6**) in THF containing 1 equiv of *tert*-butyl alcohol, suggesting that weak nucleophiles could intercept the carbene or its diazo precursor, as shown in Scheme I. It therefore seemed likely that reaction of a ketone and **5** in the presence of alcohols and amines would give enol ethers and enamines, respectively.

The outcome of efforts to reduce our expectation to practice are contained in Tables I and II (see Chart I for compound structures). The former contains the results obtained when saturated alcohols were used and the latter when saturated amines were present.[13] Several conclusions that can be drawn from these data are discussed in the succeeding paragraphs.

Nature of the Carbonyl-Containing Substrate. The conversion of saturated cyclohexanones to aldehydic enol ethers under "standard" conditions (see Experimental Section) was successful in modest to reasonably high yields (entries 1, 5, 6, 8, 9, 13–16, Table I). The examples of entries 14–16 illustrate that the transformation occurred with sterically encumbered substrates, although if camphor (entry 19) is regarded as a cyclohexanone, it is clear that steric factors can apparently suppress nucleophilic attack of the anion of the phosphonate **5** on the carbonyl function and thereby open the way for dominance of the course of reaction by what are normally minor side reactions; these may include enolization[8] but more likely involve decomposition of the phosphonate **5** or its anion.

The conversion of 2,4,4-trimethylcyclohexanone to the mixture of enol ethers **12cd** (entry 15) is of particular interest given that this ketone carries a C-2 substituent that is conformationally locked in the equatorial orientation. Harding and Tseng[14] have found such substrates to

(10) (a) Newman, M. S.; Okorodudu, A. O. M. *J. Org. Chem.* **1969**, *34*, 1220. (b) Newman, M. S.; Liang, W. C. *Ibid.* **1973**, *38*, 2438.
(11) Seyferth, D.; Marmor, R. S.; Hilbert, P. *J. Org. Chem.* **1971**, *36*, 1379.
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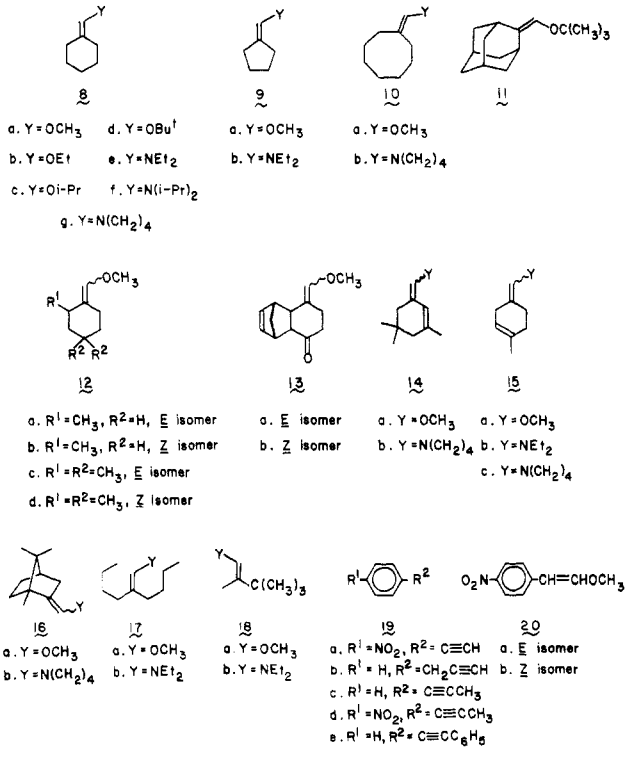
(13) The results of the corresponding reactions in which allylic alcohols and amines were used have been communicated: Gilbert, J. C.; Weerasooriya, U.; Wiechman, B.; Ho, L. *Tetrahedron Lett.* **1980**, *21*, 5003.
(14) Harding, K. E.; Tseng, C.-Y. *J. Org. Chem.* **1975**, *40*, 929.

Table II. Enamines[a]

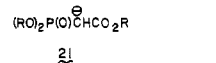
entry	substrate	amine	product[b]	% yield[c]
28	cyclohexanone	$(C_2H_5)_2NH$	8e	66 (70)[d]
29[e]	cyclohexanone	$(C_2H_5)_2NH$	8e	35
30[e,f]	cyclohexanone	$(C_2H_5)_2NH$	8e	55
31[g]	cyclohexanone	$(C_2H_5)_2NH$	8e	46
32[h]	cyclohexanone	$[(CH_3)_2CH]_2NH$	8f	50
33	cyclohexanone	pyrrolidine	8g	66
34	cyclopentanone	$(C_2H_5)_2NH$	9b	52
35	cyclooctanone	pyrrolidine	10b	55
36	3,5,5-trimethyl-2-cyclohexen-1-one	pyrrolidine	14b	0
37	4-methyl-3-cyclohexen-1-one	$(C_2H_5)_2NH$	15b	65
38	4-methyl-3-cyclohexen-1-one	pyrrolidine	15c	60
39	camphor	pyrrolidine	16b	45
40[i]	5-nonanone	pyrrolidine	17b	60
41[j]	3,3-dimethyl-2-butanone	$(C_2H_5)_2NH$	18b	50
42	benzophenone	$(C_2H_5)_2NH$	19e	97[d]

[a] The "General Procedure for Enamines" (see Experimental Section) was followed unless otherwise noted. [b] See Chart I. [c] Yields were determined by integration of ^1H NMR spectra and have not been optimized. [d] Isolated yield. [e] Reaction was conducted at 25 °C. [f] Potassium carbonate was used as the base. [g] Two equivalents of amine was used. [h] No THF was added as cosolvent. [i] Five equivalents of 5 and of potassium *tert*-butoxide. [j] Two equivalents of ketone was used; the yield is based on consumption of 5.

Chart I



be unreactive toward stabilized phosphonate anions such as **21**. The anion of **5**, which is similarly stabilized, presumably reacts with this type of ketone because of its lesser steric bulk.



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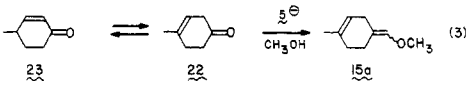
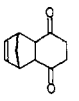
Unsaturation in the substrate was found to be permissible as long as it was β (entry 18) rather than α (entry 17) to the carbonyl group; the carbonyl carbon atom of the latter type of substrate has lessened electrophilicity, making nucleophilic attack less favorable kinetically so that side reactions again dominate. The possibility that the β,γ-unsaturated substrate **22** might be equilibrating with the α,β isomer **23**, with only the former being converted to product (eq 3), cannot be rigorously excluded as the



23 22 15a

conjugated isomer polymerizes under the reaction conditions. Nevertheless, the yield of enol ether **15a** obtained from **22** (entry 18) attests to the mildness of our reaction conditions, as the conjugated species **23** is known to be thermodynamically more stable in this system.[15] Moreover, it is known that **22** is unstable in the presence of phosphonate anions more basic than that from **5**: reaction of **1g** [$R_2 = (CH_2)_4$] with **22** led only to polymer rather than to the desired enamine **15c**.[16]

The reaction involving the dione **24** (entry 16) is noteworthy because only one of the two carbonyl functions could be made to react; i.e., treatment of monoadduct **13** with **5** under the usual reaction conditions for formation of enol ethers resulted only in recovery of starting material. It is conceivable that this is the consequence of a through-space electronic interaction between the enol ether and carbonyl moieties that significantly lessens the electrophilicity of the latter. This possibility remains to be investigated in more detail.



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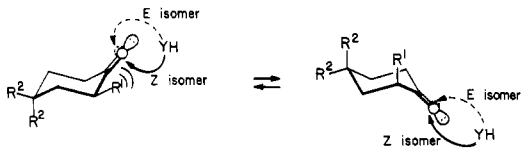
The transformation of acyclic ketones and monocyclic ketones other than cyclohexanones to the desired enol ethers has been found to be less successful. Thus, reaction conditions that afforded a 53% yield of ether **8a** from cyclohexanone (entry 1) produced yields of 33% and 0%, respectively, for cyclopentanone (entry 9) and cyclooctanone (entry 12). The acyclic ketones 5-nonanone (entry 20) and 3,3-dimethyl-2-butanone (entry 21) afforded only 20% and 36%, respectively, of the enol ethers **17a** and **18a** under conditions that gave 58% of **8a**. One possible reason for these decreased yields is discussed below.

Attempts to convert aldehydes or aromatic ketones to enol ethers failed in all examples studied (entries 22–24) with the exception of 4-nitroacetophenone (entry 25). Alkynes **19** were the major products in each case and presumably arise from the unsaturated carbene by way of a 1,2-shift of a hydride or of an aryl group.[12a,c] When the migratory aptitude of the aryl group was sufficiently poor, as with 4-nitrophenyl, the carbene could be intercepted by solvent to give enol ethers, in addition to the alkyne.

Structural dependences analogous to those described above for formation of enol ethers were observed with respect to production of enamines (Table II). For example, under "standard" conditions (see Experimental Section) a higher yield of enamine was obtained with cyclohexanone than with cyclopentanone (cf. entries 28 and 34), cyclooctanone (cf. entries 33 and 35), or acyclic ketones (cf. entries 20, 40, and 41). The reaction failed with an α,β-

(15) Lewis, K. G.; Williams, G. J. *Tetrahedron Lett.* **1965**, 4573.
(16) Martin, S. F., private communication.

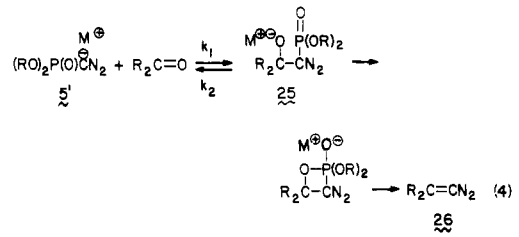
Scheme II



unsaturated ketone (entry 36) but succeeded with one that was β,γ-unsaturated (entries 37 and 38), just as before. Finally, aryl migration rather than trapping by solvent once again was the kinetically preferred fate of an appropriately substituted alkylidenecarbene (entry 42).

Comparison of Tables I and II shows that with a particular substrate the yield of enamine tended to be higher than that of enol ether. The most dramatic examples of this were the successful conversions of cyclooctanone and camphor to the corresponding pyrrolidine enamines **10b** and **16** (entries 35 and 39), whereas these ketones failed to give enol ethers (entries 12 and 19). A significant improvement in yield was also observed with cyclopentanone as the substrate (cf. entries 9 and 34).

A possible rationale for these higher yields can be based on solvation phenomena. Consider the overall reaction sequence outlined in eq 4. If it is assumed that either k_1



or k_2 is the rate-determining step, the rate of the reaction would be expected to be increased by decomplexation from each other of the ion pairs, **5′** and **25**, involved. Amines would be expected[17,18] to be more effective than alcohols at solvating the alkali cations, viz., lithium and potassium, present in our reactions. Their presence, therefore, should enhance the rate of production of the key intermediate, the diazoethene **26** (eq 4), relative to the corresponding reaction in alcoholic media. Facilitation of the 1,2-addition process to the carbonyl function would lessen the importance of side reactions that result in unproductive consumption of **5**.

Apart from the evaluation of overall yields of product as a function of the structure of the carbonyl substrate, the use of several unsymmetrically substituted ketones as substrates has yielded some data regarding E/Z ratios of products. Conversion of 3,3-dimethyl-2-butanone to an enol ether (entry 21) or an enamine (entry 41) afforded the E isomer **18** exclusively, as judged by analysis of the ^{1}H NMR spectrum of the crude reaction mixture. When cyclohexanones having a single C-2 substituent were used, formation of the E isomer was stereoselective by a factor ranging from 2 to 10. The higher value was obtained with 2,4,4-trimethylcyclohexanone (entry 15), in which the C-2 methyl group, as noted earlier, occupies the equatorial position.

These stereochemical results are consistent with the mechanistic notion that the trajectory of attack of the nucleophile on the alkylidenecarbene is in a plane orthogonal to that defined by the π system, as shown in Scheme II. A substituent, R, in or near this plane would hinder attack from that side and therefore favor formation of the E isomer.

Nature of the Nucleophile. The steric environment about the nucleophilic atom involved in trapping the carbene appears not to be of significance in defining yields, although this aspect of the reaction has not been thoroughly investigated. Enol ethers can be made in good yields even with tertiary alcohols (entries 8 and 13), and both diethyl- and diisopropylamine were effective for the production of enamines (entries 28 and 32) although the yield of product from the more sterically hindered amine was somewhat lower.

Nature of the Base. Potassium *tert*-butoxide has been the principal base used in this work, although in alcoholic media it obviously served only as a convenient way to produce the alkoxide of the particular alcohol being used. Other bases such as potassium carbonate and lithium hydroxide (entries 4, 7, 14, 18, 30) appeared to have comparable effectiveness. The poor solubility of the carbonate in the reaction media did result in slower rates of reaction, but its use might be of advantage with ketonic substrates that are particularly base labile. A similar solubility factor required an extended reaction time in the case when lithium hydroxide was used (entry 7).

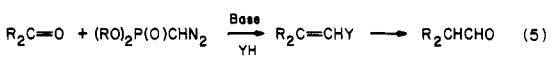
Optimization of Yield. Although an extended effort has not been made to optimize the yields of either enol ethers or enamines, some general comments can be made. First, the temperature at which the reaction was performed seemed to make little difference in the yield of enol ethers (cf. entries 1 and 2 and entries 9 and 10) but appeared to do so in the case of enamines, lower temperatures affording increased yields (cf. entries 28 and 29); use of potassium carbonate did allow preparation of enamines efficiently at room temperature, although extended reaction times were then required (entry 30).

Second, the use of a larger excess of the (diazomethyl)phosphonate **5** resulted in increased yields (cf. entries 1 and 3). In this connection it is to be noted that 5 equiv of **1e** were used by Corey and Tius in their synthesis of enol ethers.[8]

Although the effect on yield of the concentration of alcohol has not been studied, such an effect was seen for enamines. Comparison of entries 28 and 31 reveals a significant decrease in yield in going from an 18-fold to a 2-fold excess of the amine.

Conclusion

The reaction of the phosphonate **5** with aliphatic ketones in the presence of alcohols and amines represents a mild synthetic method for preparation of aldehydic enol ethers and enamines. Given that these products are readily converted to the corresponding aldehydes,[3,19] **5** represents a new reagent of value for achieving reductive nucleophilic formylation of ketones (eq 5).[4] In addition, the fact that



a variety of enol ethers and enamines can be prepared from a single phosphorus-containing reagent provides synthetic flexibility unprecedented in such reagents.

Experimental Section

Proton magnetic resonance (^{1}H NMR) spectra were obtained by using either a Varian A-60 or a Varian HA-100 spectrometer.

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The corresponding carbon (^{13}C NMR) spectra were taken with a Varian FT80-A instrument. Chemical shifts are reported in parts per million downfield from Me_4Si as an internal reference at 0.00 ppm. Coupling constants (J) are reported in hertz. Ratios of areas of absorptions were obtained by averaging at least two successive integrations. Unless otherwise noted, ^1H NMR data are for solutions in CCl_4 and are reported in the following manner: parts per million downfield from Me_4Si, multiplicity, coupling constant if applicable, number of protons, and the carbon atom(s) to which the hydrogen atom(s) are attached (if known). ^{13}C NMR data are for samples in $CDCl_3$.

Infrared (IR) spectra, unless noted otherwise, were taken of neat samples held between salt plates with either a Beckman IR-54 or Acculab-8 spectrophotometer. All absorptions are reported in units of reciprocal centimeters and are calibrated to the absorption at 1601 cm^{-1} of polystyrene.

Determinations of accurate mass were made on a Du Pont 21-210 high-resolution mass spectrometer operating at 70 eV; medium-resolution spectra were obtained with a Du Pont 21-471 instrument using the same ionizing voltage.

Melting points were taken on samples contained in open capillary tubes and are uncorrected.

Standard Procedure for Preparation of Enol Ethers. A solution containing 1 mmol of ketone and 1.1 mmol of dimethyl (diazomethyl)phosphonate (**5**)[11] in 50–100 mmol of anhydrous alcohol was placed in a dry flask containing a magnetic stirring bar and equipped so that a static atmosphere of dry nitrogen could be maintained throughout the course of the reaction. Subsequently, a solution of 1.2 mmol of potassium *tert*-butoxide in 70 mmol of anhydrous alcohol was added over a 2-min period with stirring. The reaction mixture was stirred at ambient temperatures for 2 h after which 25 mL of water was added. The resulting solution was extracted three times with 20-mL portions of pentane, and the combined organic extracts were washed twice with 25-mL quantities of brine and dried (Na_2SO_4). Pentane and excess alcohol were removed by rotary evaporation, a measured quantity of benzene was added to the residue to serve as an internal standard, and the entire solution was then transferred to an NMR tube for analysis. Pure products were isolated by either vacuum distillation or GLC purification.

(Methoxymethylene)cyclohexane (8a).[10a] This product was characterized by comparison of its ^1H NMR and IR spectra with those reported.[20]

Low-Temperature Reaction (Entry 2). A flask equipped as above and containing a solution of potassium *tert*-butoxide (250 mg, 2.2 mmol) in anhydrous methanol (1.0 mL, 25 mmol) was cooled to −78 °C. A solution of phosphonate **5** (300 mg, 2.0 mmol) in methanol (2.0 mL, 50 mmol) was added dropwise over a period of 1 min, and the resulting mixture was stirred for 5 min. Next, cyclohexanone (200 mg, 2.0 mmol) in methanol (2.0 mL, 50 mmol) was introduced in a dropwise fashion over 1 min, and this mixture was stirred at −78 °C for 10 h and at room temperature for 5 h. The workup followed the standard procedure.

Excess Phosphonate (Entry 3). The standard procedure was followed except that 2.2 mmol of **5** and of potassium *tert*-butoxide were used.

Potassium Carbonate (Entry 4). The standard procedure was followed except that 2.0 mmol of anhydrous potassium carbonate was used in place of potassium *tert*-butoxide.

(Ethoxymethylene)cyclohexane (8b):[10a,20a] ^1H NMR δ 1.20 (3 H, t, J = 7.0 Hz, CH_3), 1.35–1.65 (6 H, m, aliphatic CH_2), 1.70–2.40 (4 H, m, allylic CH_2), 3.65 (2 H, q, J = 7.0 Hz, OCH_2), 5.70 (^1H, m, vinylic CH); IR 1680 cm^{-1} (C=C); mass spectrum, m/e 140 (molecular ion, base peak).

(2-Propoxymethylene)cyclohexane (8c):[10a,20a] ^1H NMR 1.15 (6 H, d, J = 6.0 Hz, CH_3), 1.30–1.70 (6 H, m, aliphatic CH_2), 1.70–2.30 (4 H, m, allylic CH_2), 3.7 (1 H, m, J = 6.0 Hz, OCH), 5.7 (1 H, m, vinylic CH); IR 1690 cm^{-1} (C=C); exact mass 154.1361 (calcd for $C_{10}H_{18}O$ 154.1358).

Lithium Hydroxide (Entry 7). The standard procedure was followed except that lithium hydroxide instead of potassium *tert*-butoxide was used, and the reaction mixture was stirred for 12 h.

(*tert*-Butoxymethylene)cyclohexane (8d).[10a] This product was identified by comparison of its ^1H NMR, IR, and mass spectra with those published.[20a,21]

(Methoxymethylene)cyclopentane (9a):[10a,20a] ^1H NMR δ 1.40–1.80 (4 H, m, aliphatic CH_2), 1.90–2.30 (4 H, m, allylic CH_2), 3.40 (3 H, s, OCH_3), 5.75 (1 H, m, vinylic CH); IR (CCl_4) 1690 cm^{-1}; exact mass 112.0889 (calcd for $C_7H_{12}O$ 112.0888).

Low-Temperature Reactions (Entries 10 and 11). The procedure at −78 °C described for (methoxymethylene)cyclohexane was used for entry 10. In the case of entry 11, the reaction mixture was initially stirred at −100 °C for 1 h, after which the procedure described for the −78 °C reaction was followed.

2-(*tert*-Butoxymethylene)adamantane (11): ^1H NMR 1.20 (9 H, s, CH_3), 1.60–1.80 (12 H, m, alicyclic CH), 2.10–2.34 (1 H, m, allylic CH), 2.80–3.10 (1 H, m, allylic CH), 5.85 (1 H, s, vinylic CH); exact mass 220.1824 (calcd for $C_{15}H_{24}O$ 220.1827).

(*E*)- and (*Z*)-1-(Methoxymethylene)-2-methylcyclohexane (12a,b): ^1H NMR δ 0.98, 1.02 (3 H, 2 d, J = 6.5, 7.5 Hz, CCH_3), 1.30–2.70 (9 H, m, alicyclic CH), 3.45, 3.48 (3 H, 2 s, OCH_3), 5.60 (1 H, m, vinylic CH); IR (CCl_4) 1685 cm^{-1} (C=C); exact mass 140.1203 (calcd for $C_9H_{16}O$ 140.1201).

(*E*)- and (*Z*)-4-(Methoxymethylene)-1,1,3-trimethylcyclohexane (12c,d): ^1H NMR δ 0.85 (6 H, br s, C-1, CH_3), 0.90 (3 H, d, J = 6.0 Hz, C-3 CH_3), 1.4–2.8 (7 H, m, alicyclic CH), 3.40, 3.45 (3 H, 2 s, OCH_3), 5.50, 5.60 (1 H, 2 m, vinylic CH); exact mass 168.1519 (calcd for $C_{11}H_{20}O$ 168.1514).

(*E*)- and (*Z*)-8-(Methoxymethylene)-*endo*-1,4,4a,6,7,8a-hexahydro-1,4-methanonaphthalen-5-one (13a,b). This reaction was performed at 0 °C. Spectral data (major isomer, believed to be **13a**, only): ^1H NMR δ 1.23 (2 H, m, H-9), 2.03 (4 H, br s, H-6, H-7), 2.73 (1 H, dd, H-8a), 3.10–3.55 (3 H, m, H-1, H-4, H-4a), 3.58 (3 H, s, OCH_3), 5.87 (1 H, m, C=C(OR)H), 6.00 (2 H, m, HC=CH); ^{13}C NMR ($CDCl_3$) 25.77, 38.45, 41.90, 46.94, 48.37, 49.09, 51.57, 59.56 (OCH_3) 115.0 (C-8), 136.0 (C-2 or C-3), 137.2 (C-2 or C-3), 142.5 (C-10), 213.3 (C-5); IR 1700 (C=O), 1660 cm^{-1} (C=C); exact mass 204.1154 (calcd for $C_{13}H_{16}O_2$; 204.1150).

4-(Methoxymethylene)-1-methyl-1-cyclohexene (15a). The precursor ketone was prepared by the method of Corey and Watt.[22] The enol ether **15a** was shown to have ^1H NMR, IR, and mass spectra identical with those reported.[23]

(*E*)-2,3,3-Trimethyl-1-methoxy-1-butene (18a). The low-temperature procedure described for (methoxymethylene)cyclohexane was used. The reaction mixture was held at −78 °C for 24 h prior to the workup. The ^1H NMR, IR, and mass spectra corresponded to those previously reported for **18a**.[10b] The stereochemical assignment is based on the observation of a 1.2-Hz coupling constant between the vinylic hydrogen and the C-2 methyl group; the magnitude of this is consistent with an *E* rather than a *Z* relationship.[24] No resonances attributable to the *Z* isomer could be detected.

2-(1-Butyl)-1-methoxy-1-hexene (17a): ^1H NMR 0.90 (6 H, m, aliphatic CH_3), 1.00–1.55 (8 H, m, aliphatic CH_2), 1.60–2.20 (4 H, m, allylic CH_2), 3.45 (3 H, s, OCH_3), 5.65 (1 H, m, vinylic CH); IR 1685 cm^{-1} (C=C); mass spectrum, m/e 170 (M^+), 127 ($M - n\text{-}C_3H_7$), 85 (base peak); exact mass 170.1668 (calcd for $C_7H_{12}O$ 170.1671).

Standard Procedure for Preparation of Enamines. A dispersion of 1.3 mmol of potassium *tert*-butoxide in 0.5 mL of anhydrous THF and 18 mmol of freshly distilled amine, contained in a flask equipped as before, was cooled to −78 °C, and a solution of 1.2 mmol of phosphonate **5** in 1 mL of THF was added dropwise. After this mixture had been stirred for 5 min, 1.0 mmol of ketone in 1.5 mL of THF was introduced over a 1-min period, and the solution that resulted was stirred at −78 °C for 12 h. The solution was brought to room temperature, and solvents were removed by rotary evaporation. The residue was washed twice with 10-mL portions of ether, and the combined extracts were subjected to rotary evaporation. Analysis by ^1H NMR of the

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residue, to which benzene had been added as an internal standard, gave the reported yields. Pure enamines were obtained by vacuum-transfer techniques.

[(Diethylamino)methylene]cyclohexane (8e): ^{1}H NMR δ 0.95 (6 H, t, J = 7.0 Hz, CH_3), 1.30–1.70 (6 H, m, aliphatic CH_2), 2.00 (2 H, m, allylic CH_2), 2.25 (2 H, m, allylic CH_2), 2.45 (4 H, q, J = 7.0 Hz, NCH_2), 4.95 (1 H, m, vinylic CH); IR 1670 cm^{-1} (C=C); exact mass 167.1671 (calcd for $C_{11}H_{21}N$ 167.1674).

Room-Temperature Reaction (Entries 29 and 30). The standard procedure was followed (entry 29) except that the diazophosphonate and the ketone were added together and that the reaction was terminated after 5 min as gas evolution had ceased. The added modifications of substituting 2 equiv of **5** and of potassium carbonate per equivalent of cyclohexanone and of extending reaction time to 40 h were made to obtain the data of entry 30.

[(Diisopropylamino)methylene]cyclohexane (8f): ^{1}H NMR δ 0.90 (12 H, d, J = 6.3 Hz, CH_3), 1.30–1.70 (6 H, m, aliphatic CH_2), 1.80–2.40 (4 H, m, allylic CH_2), 2.95 (2 H, m, J = 6.3 Hz, NCH), 5.20 (1H, m, vinylic CH); IR 1660 cm^{-1} (C=C); exact mass 195.1991 (calcd for $C_{13}H_{25}N$ 195.1987).

(Pyrrolidinylmethylene)cyclohexane (8g). This product had ^{1}H NMR, IR, and mass spectra corresponding to those reported.[25]

[(Diethylamino)methylene]cyclopentane (9b): ^{1}H NMR δ 0.95 (6 H, t, J = 6.5 Hz, CH_3), 1.40–1.90 (4 H, m, aliphatic CH_2), 2.00–2.40 (4 H, m, allylic CH_2), 2.72 (4 H, q, J = 6.5 Hz, NCH_2), 5.35 (1 H, m, vinylic CH); IR 1660 cm^{-1} (C=C); exact mass 153.1520 (calcd for $C_{10}H_{19}N$ 153.1517).

(Pyrrolidinylmethylene)cyclooctane (10): ^{1}H NMR δ 1.30–2.40 (18 H, m, alicyclic CH_2), 2.70–3.10 (4 H, m, NCH_2), 5.50 (1 H, m, vinylic CH); IR (CCl_4) 1660 cm^{-1}; exact mass 193.1835 (calcd for $C_{13}H_{23}N$ 193.1830).

4-[(Diethylamino)methylene]-1-methyl-1-cyclohexene (15b): ^{1}H NMR δ 0.95 (6 H, t, J = 7.0 Hz aliphatic, CH_3), 1.60 (3 H, br s, allylic CH_3), 1.70–2.85 (10 H, m, alicyclic CH_2 and NCH_2), 5.10 (1 H, m, C=C[C]H), 5.25 (1 H, m, C=C[NR_2]H); exact mass 179.1677 (calcd for $C_{12}H_{21}N$ 179.1674).

4-(Pyrrolidinylmethylene)-1-methyl-1-cyclohexene (15c). The ^{1}H NMR, IR, and mass spectra of this enamine corresponded to those reported.[26]

2-(Pyrrolidinylmethylene)-1,7,7-trimethylbicyclo[2.2.1]heptane (16b).[27] The standard procedure was followed except that 4 equiv of base and 4 equiv of phosphonate were used: ^{1}H NMR 0.76 (3 H, s, *syn*-C-7 CH_3 [?]), 0.87 (6 H, br s, C-1 and *anti*-C-7 CH_3 [?]), 1.10–1.95 (11 H, 2 m, alicyclic CH_2, CH), 3.00 (4 H, m, NCH_2), 5.44 (1 H, t, vinylic CH); IR 1670 cm^{-1} (C=C); exact mass 219.1989 (calcd for $C_{15}H_{25}N$ 219.1987). The presence of a second triplet at δ 5.27 in the ^{1}H NMR spectrum indicates that the enamine may be a mixture of diastereomers in a ratio of ca. 4:1.

The enamine was further characterized by hydrolysis to the corresponding aldehyde which had a ^{13}C NMR spectrum consonant with that reported[28] and afforded a semicarbazone having the necessary melting point [mp 204.5–205.2 °C, after two recrystallizations from methanol/water (lit.[29] mp 203.5–204 °C)].

2-Butyl-1-pyrrolidinyl-1-hexene (17b): ^{1}H NMR 0.80–1.10 (6 H, m, CH_3), 1.10–2.35 (16 H, m, aliphatic CH_2), 2.65–3.10 (4 H, m, NCH_2), 5.45 (1 H, m, vinylic CH); IR (CCl_4) 1650 cm^{-1}; exact mass 209.2147 (calcd for $C_{14}H_{27}N$ 209.2143).

1-(Diethylamino)-2,3,3-trimethyl-1-butene (18b): ^{1}H NMR δ 1.0 (6 H, t, J = 7.0, CH_3), 1.02 (9 H, s, $C(CH_3)_3$), 1.68 (3 H, d, J = 1.2 Hz), 2.45 (4 H, q, J = 7.0 Hz, CH_2), 5.05 (1 H, m, vinylic CH); IR 1660 cm^{-1}; exact mass 169.1835 (calcd for $C_{11}H_{23}N$ 169.1830).

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Registry No. **5**, 27491-70-9; **8a**, 19096-89-0; **8b**, 19684-50-5; **8c**, 19684-52-7; **8d**, 19684-53-8; **8e**, 69762-72-7; **8f**, 76886-47-0; **8g**, 6815-55-0; **9a**, 19684-48-1; **9b**, 76886-48-1; **10a**, 84175-83-7; **10b**, 76902-54-0; **11**, 68251-99-0; **12a**, 84175-84-8; **12b**, 84175-85-9; **12c**, 84175-86-0; **12d**, 84175-87-1; **13a**, 84175-88-2; **13b**, 84236-35-1; **14a**, 84175-89-3; **14b**, 84175-90-6; **15a**, 66334-24-5; **15b**, 84175-91-7; **15c**, 64715-27-1; **16a**, 76713-57-0; **16b**, 84175-92-8; **17a**, 73314-70-2; **17b**, 84175-93-9; **18a**, 76886-46-9; **18b**, 84175-94-0; **19a**, 937-31-5; **19b**, 10147-11-2; **19c**, 673-32-5; **19d**, 28289-83-0; **19e**, 501-65-5; **20a**, 66821-16-7; **20b**, 66821-15-6; CH_3OH, 67-56-1; CH_3CH_2, 64-17-5; $(CH_3)_2CHOH$, 67-63-0; $(CH_3)_3COH$, 75-65-0; $(C_2H_5)_2NH$, 109-89-7; $[(CH_3)_2CH]_2NH$, 108-18-9; pyrrolidine, 123-75-1; cyclohexanone, 108-94-1; cyclopentanone, 120-92-3; cyclooctanone, 502-49-8; adamantanone, 700-58-3; 2-methylcyclohexanone, 583-60-8; 2,4,4-trimethylcyclohexanone, 2230-70-8; *endo*-1,4,4a,6,7,8a-hexahydro-1,4-methanonaphthalene-5,8-dione, 32061-93-1; 3,5,5-trimethyl-2-cyclohexen-1-one, 78-59-1; 4-methyl-3-cyclohexen-1-one, 5259-65-4; camphor, 76-22-2; 5-nonanone, 502-56-7; 3,3-dimethyl-2-butanone, 75-97-8; 4-nitrobenzaldehyde, 555-16-8; 2-phenylethanal, 122-78-1; acetophenone, 98-86-2; 4-nitroacetophenone, 100-19-6; benzophenone, 119-61-9.

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