Charge-Directed Conjugate Addition Reactions in the Preparation of Substituted Methyl Ketones

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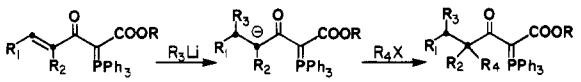
Charge-directed conjugated addition reactions of the *tert*-butyl esters of α,β-unsaturated acylphosporanes **2** have been used to prepare a variety of substituted methyl ketones. Substituted ylides **6** are prepared by alkylating ylide anions **4** generated by the addition of nucleophiles to **2** and are converted under acidic conditions to substituted (acylmethylene)phosphoranes **12** which are hydrolyzed to methyl ketones. The utility of these unsaturated acylphosphoranes as methyl vinyl ketone equivalents in conjugate addition–alkylation reactions is demonstrated in a synthesis of the racemic form of the sex pheromone of the California red scale, **14**.

We recently described a new approach to the functionalization of α,β-unsaturated carbonyl-containing systems through what we have termed charge-directed conjugate addition reactions.[1] In this approach carbonyl additions by nucleophiles are suppressed by the interaction of the carbonyl group with a proximal unit of charge, thereby favoring the 1,4-mode of addition. Unsaturated acyl ylides have been found to be especially useful in this regard (eq 1). The addition of a wide range of nucleophiles to **1** gives



(1)

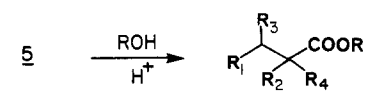
1 R=Et **3** R=Et **5** R=Et

2 R=t-Bu **4** R=t-Bu **6** R=t-Bu

a $R_1 = R_2 = H$ **b** $R_1 = Me, R_2 = H$ **c** $R_1 = Ph, R_2 = H$

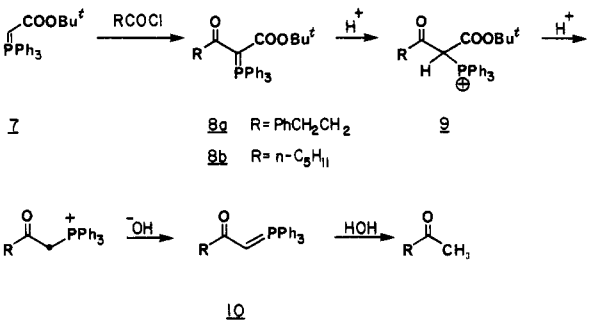
reactive ylide anions **3** which are readily alkylated by ordinary alkyl halides.[1] The required Michael acceptors are in general readily prepared either from the corresponding acid chloride and the appropriate (triphenylphosphoranylidene)acetate or by Wittig–Horner olefination.[2] Highly stabilized ylides such as **1** and **5** are usually quite stable, relatively nonpolar, and easily purified by chromatography. In contrast to the cuprate approach to such functionalizations,[3] nucleophiles ranging from alkyllithium reagents to ester enolates have been found to undergo the addition process with **1**, giving reactive ylide anions **3** whose utility is not limited to only reactions with the more reactive alkylating agents. In addition, substitution is generally well tolerated in acceptor **1** where conjugate addition reactions readily occur, except in cases involving intermolecular additions to β,β-disubstituted acceptors.[4] We have also shown that intramolecular additions and alkylations may be used for the construction of five- and six-membered carbocycles.[5]

In order to be of synthetic utility, the product ylides derived from the addition–alkylation process must be readily converted into more useful classes of organic compounds. To this end we have previously reported that under acidic conditions ylide **5** undergoes alcoholysis to give esters in high yields[1] (eq 2). This transformation



(2)

Scheme I



allows unsaturated ylide **1** to serve as an acrylate equivalent in conjugate addition–alkylation reactions and provides a versatile source of the $R_1C^+HC^-HR_2COOR$ synthon. Simple functional group transformations resulting in the formation of highly functionalized ketones would likely be of even greater synthetic value. In this paper we report on the use of unsaturated ylide acceptor **2** as a methyl vinyl ketone equivalent in charge-directed conjugate addition–alkylation reactions where it functions as sources of a $R_1C^+HC^-HR_2COCH_3$ synthon in the preparation of substituted methyl ketones. In the accompanying paper we also describe a versatile route to more highly substituted ketones from ylides obtained from conjugate addition–alkylation reactions.

Results and Discussion

Decarbalkoxylation of *tert*-Butyl Ylide Esters. While the carbanionic center present in the ylide moiety of **1** serves well its intended purpose of charge protecting adjacent carbonyl groups against attack by nucleophiles, this feature largely precludes the use of many of the usual methods employing bases or nucleophiles for the subsequent manipulation of the carbonyl groups in **5**. Protonation of the weakly basic carbanionic center removes this protection, however, but only carbonyl reactions involving weakly basic nucleophiles, as in the alcoholysis to esters (eq 2), are effective, owing to the ease of regenerating the highly stabilized ylide through deprotonation. We decided, therefore, to investigate the possibility of using the corresponding *tert*-butyl esters **6**, anticipating that such esters could be converted to the corresponding carboxylic acid under acidic conditions with subsequent decarboxylation to give stabilized (acylmethylene)phosphoranes **10** which are known to be readily hydrolyzed to methyl ketones under mild conditions[6] (Scheme I).

The ease of affecting the required decarbalkoxylation was initially studied by NMR spectroscopy using model

(1) Cooke, M. P., Jr.; Goswami, R. *J. Am. Chem. Soc.* **1977**, *99*, 642.
(2) Cooke, M. P., Jr.; Biciunas, K. P. *Synthesis* **1981**, 283.
(3) Posher, G. H. *Org. React.* **1972**, *19*, 1.
(4) A number of intramolecular additions have been observed recently: unpublished results with R. K. Widener.
(5) Cooke, M. P., Jr. *Tetrahedron Lett.* **1979**, 2199.
(6) Cooke, M. P., Jr. *J. Org. Chem.* **1973**, *38*, 4082.

0022-3263/82/1947-4955$01.25/0

Table I. Substituted Ylides 6 from Addition-Alkylation Reactions of 2 (Eq 1)

					6[a]				
entry	compd	R_1 for 2[a]	R_3Li	R_4X	product	R_1	R_3	R_4	yield, %
1	2a	H	*n*-BuLi	MeI	6a	H	*n*-Bu	Me	96
2		H	*n*-BuLi	*n*-AmI	6b	H	*n*-Bu	*n*-Am	83
3		H		MeI	6c	H		Me	84
4		H	PhLi	H_2O	6d	H	Ph	H	75
5		H	PhLi	*n*-PrI	6e	H	Ph	*n*-Pr	98
6	2b	Me	PhLi	$PhCH_2Br$	6f	Me	Ph	$PhCH_2$	84
7	2c	Ph	MeLi	$PhCH_2Br$	6f	Me	Ph	$PhCH_2$	99
8	2b	Me	*n*-BuLi	$PhCH_2Br$	6g	Me	*n*-Bu	$PhCH_2$	98
9	2c	Ph	*n*-BuLi	MeI	6h	Ph	*n*-Bu	Me	98

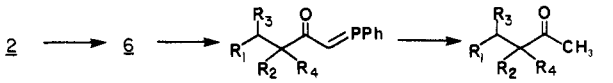
[a] R_2 = H in all cases.

ylides 8. Debutylation was not observed when a solution of **8a**, in either chloroform containing 1 equiv of trifluoroacetic acid (TFA) or benzene containing 2 equiv of *p*-toluenesulfonic acid, was heated at 50 °C for 4 h. Debutylation was observed in the presence of larger quantities of acid, however. With 5 equiv of TFA in chloroform, nearly complete disappearance of **8a** occurred in 8 h at 50 °C, while a similar result was obtained in benzene solution in less than 5 h. It was our hope that an intramolecular interaction between the electrophilic phosphonium group and the ester carbonyl group in **9** would facilitate the desired loss of the *tert*-butyl group enabling the reaction to occur at low acid concentrations. No such effect seems to be operative, however, and the results suggest that debutylation requires a further protonation of phosphonium salt **9**. Hydrolysis of resulting (acylmethylene)-phosphoranes **10** under standard (but not optimized) conditions (vide infra) and subsequent product analysis by GLC confirmed the superiority of benzene over chloroform as a reaction solvent. An 88% yield of benzylacetone was obtained in the former case and a 70% yield in the latter. Several solvents were found to be less effective. Heating **8b** in the more basic solvent THF with 5 equiv of TFA for 4 h at 50 °C was without effect. Slow debutylation was observed in 3 h when **8a** was heated at 50 °C in methanol containing 6 equiv of aqueous HCl, but hydrolysis of the product resulting from heating **8b** with 1.5 equiv of aqueous HCl in ethanol gave, in addition to 2-heptanone (64%), ethyl hexanoate. Under these conditions acyl attack in **9** by the solvent competes with the desired debutylation when alcohols are used as the reaction medium.

Successful debutylations with TFA in benzene led us to try the use of TFA alone as the reaction medium. NMR experiments revealed that complete debutylation of **8a** requires 70 h at 25 °C with neat TFA but is complete in 0.5 h at 50 °C. The yields of benzylacetone and 2-heptanone, resulting from the subsequent standard hydrolysis of ylides **10**, obtained upon heating **8a** and **8b** in TFA at 50 °C for 0.75 h, were found by GLC to be 92% and 89%, respectively. While the use of TFA was quite satisfactory for affecting the desired decarbalkoxylation, a less acidic medium, acetic acid, was found to be equally satisfactory. Heating **8b** in glacial acetic acid for 30 h at 90 °C gave, ultimately, 2-heptanone in 93% yield. A slightly lower yield was obtained after only 20 h at 90 °C (83%) while no reaction was observed after 4 h at 50 °C.

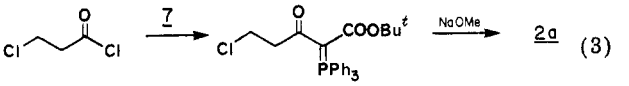
Methyl Ketones from Unsaturated Acyl Ylides. With procedures in hand for the conversion of ylides such as 8 to methyl ketones, we examined the charge-directed conjugate addition reactions of unsaturated ylides **2** as a source of substituted methyl ketone precursor **6**. The

Scheme II



12 **13**

required unsaturated ylides are readily prepared from the corresponding acid chloride, as shown in Scheme I, except in the case of unsubstituted ylide **2a**. In this case, as has been our general experience,[1] the use of acryloyl chloride results in low yields of the desired ylide, and the method shown in eq 3 was found to be more satisfactory. The



(3)

11

β-chloro ylide **11**, obtained from 3-chloropropanoyl chloride and **7** in 91% yield, readily undergoes dehydrochlorination with $NaOCH_3$ to give **2a** in 74% yield.

The addition–alkylation reactions of **2** were uneventful. The addition of a variety of nucleophiles to **2** gave the corresponding ylide anion **4** which, upon reaction with electrophiles, gave good yields of substituted ylides **6** as shown in Table I. The purification of reaction products was readily accomplished by chromatography on silica gel, though in many cases the crude reaction product could be used directly without further purification. Substituted ylides **6** were then converted to the corresponding methyl ketone as outlined in Scheme II, and reaction conditions and product yields for these transformation are shown in Table II.

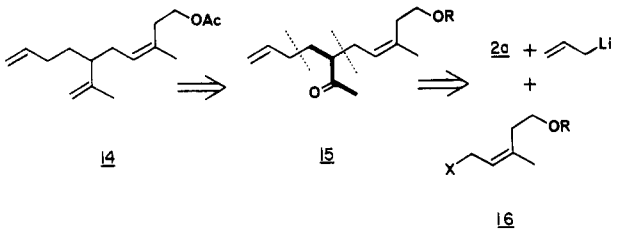
Decarbalkoxylations were conducted by heating **6** in either TFA at 50–55 °C (method A) or in glacial acetic acid at 90 °C (method B). In general, both methods gave good results, the notable exception being in the case of entry 3 where presence of the dithiane moiety was observed to be incompatible with the use of TFA (method A). The use of HOAc (method B) in this case gave satisfactory results. Neutralization of the crude reaction products, obtained from either procedure, gave corresponding (acylmethylene)triphenylphosphoranes **12** which were heated, without isolation, in aqueous ethanol at pH 8–10, giving good yields of substituted methyl ketones **13**. Optimum hydrolysis times were found to vary with the structure of **12**, and, in general, maximum yields were obtained after heating for 12–14 h in cases where the acylphosphorane contained no α substituent (**12**, $R_2 = R_4 = H$) and after 20–40 h in cases where an α substituent was present.

Table II. Methyl Ketones 13 from Substituted Ylides 6

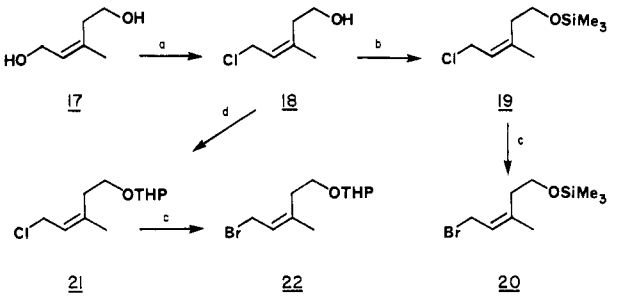
entry	ylide	hydrolysis method[a]	reaction time with RCOOH, h	EtOH-H_2O hydrolysis time, h	13[e] R_1	R_3	R_4	yield,[b] %
1	6a	A	1	12	H	*n*-Bu	Me	65[c]
		A	1	16				(90)[c,d]
		B	30	15				48[d]
2	6b	A	0.75	22	H	*n*-Bu	*n*-Am	83
		B	31.5	22				73[d]
3	6c	A	0.75	22	H		Me	0
		B	30	22				65
4	6d	A	0.75	41	H	Ph	H	(90)[c]
		B	30.5	42				(89)[d]
5	6e	A	0.75	40	H	Ph	*n*-Pr	86
6	6f	A	1	43	Me	Ph	$PhCH_2$	50
7	6g	A	1	42	Me	*n*-Bu	$PhCH_2$	80
8	6h	A	1	42	Ph	*n*-Bu	Me	91
9	8b	A	0.75	13.5	H	*n*-Pr	H	(92)[c]
		B	20	12.5				(93)

[a] Method A: TFA, 50–55 °C followed by EtOH-H_2O, pH 8–10, reflux. Method B: HOAc, 90 °C followed by EtOH-H_2O, pH 8–10, reflux. [b] Isolated yields. GLC yields are in parentheses. [c] The structure of the known ketone was confirmed through the melting point of its 2,4-dinitrophenylhydrazone. [d] Overall yield from 2 without purification of 6. [e] R_2 = H in all cases.

Scheme III

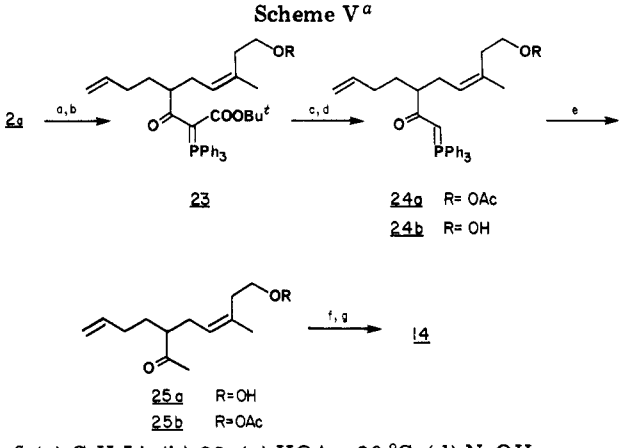


Scheme IV[a]



[a] (a) Me_2S, NCS; (b) $(Me_3Si)_2NH$, Me_3SiCl; (c) NaBr, NMP; (d) DHP, HCl.

Scheme V[a]



[a] (a) C_3H_5Li; (b) 22; (c) HOAc, 90 °C; (d) NaOH; (e) EtOH-H_2O-H_2O, 70 °C; (f) Ac_2O, Py; (g) CH_2=PPh_3.

Entries 1, 2, and 4 illustrate the direct conversion of unsaturated ylide **2** to substituted methyl ketones **13** without the purification of any intermediates. Through the sequence shown in Scheme II, **2** therefore serves as a versatile source of substituted methyl vinyl ketones equivalents in conjugate addition–alkylation reactions. It is especially noteworthy that in addition to the forementioned advantages offered by the charge-directed conjugate addition approach, methyl vinyl ketone often gives poor results in conjugate addition reactions with organocuprates.[7]

Synthesis of the California Red Scale Sex Pheromone. In order to examine the synthetic utility of this methodology, the synthesis of the racemic form of **14**, the sex pheromone of the California red scale,[8] was undertaken[9] in the manner suggested by the retrosynthetic analysis shown in Scheme III. Intermediate **15** possesses the methyl ketone which arises from our conjugate addition–alkylation methodology and requires only the addition of allyllithium to **2a** with subsequent alkylation of the intermediate ylide anion **4** (R_1 = allyl) with an electrophilic fragment such as **16** for nearly complete assembly of the carbon skeleton. Furthermore, model experiments using the acetate of (*E*)-3-methyl-2-hexen-5-ol[10] suggested that the debutylation procedure needed to unmask the methyl ketone unit in the fully alkylated ylide (method B, Table II), would be compatable with the functionality introduced through **16**. NMR analysis[10] of the recovered model acetate indicated that no chemical or stereochemical damage to the homoallylic unit had occurred upon heating it for several hours in HOAc at 90 °C.

We initially chose previously reported protected allylic chloride **19**,[11] prepared as shown in Scheme IV, for use as the alkylation agent leading to **23** in Scheme V. (*Z*)-Chlorohydrin **18**, containing less than 2% of its *E* isomer, was prepared as described by Corey[11] by spinning-band

(7) Jacob, P., III; Brown, H. C. *J. Am. Chem. Soc.* **1976**, *98*, 7832 and references cited therein.

(8) (a) Roelofs, W. L.; Gieselmann, M. J.; Cardé, A. M.; Tashiro, H.; Moreno, D. W.; Henrick, C. A.; Anderson, R. S. *Nature (London)* **1977**, *267*, 698. (b) *J. Chem. Ecol.* **1978**, *4*, 211.

(9) For previous syntheses see Reference 8b and Still, W. C.; Mitra, A. *J. Am. Chem. Soc.* **1978**, *100*, 1927.

(10) Cooke, M. P., Jr. *J. Org. Chem.* **1979**, *44*, 2461.

(11) Corey, E. J.; Kim, C. V.; Takeda, M. *Tetrahedron Lett.* **1972**, 4339.

Table III. Geranyl Bromide from Geranyl Chloride and Metal Halides[a]

entry	metal halide	solvent	metal halide/geranyl chloride ratio	reaction time, h	temp, °C	% geranyl bromide[b,c]	% olefin isomerization[c]
1	LiBr	THF	4	4	20	88	22
2			11	4		>98	55
3			4	4	65	84	16
4			7	5		91	20
5		acetone	4	4	20	77	
6		MeCN	4	4		75	
7			11	4		87	
8	NaBr	acetone	4	3		4	
9		MeCN	4	3		4	
10		NMP	11	0.25		79	
11				0.5		87	
12				1.5		95	<1
13				3.0		95	<1
14				7.5		95	2
15			4	3		93	2
16				7		92	2
17			2	3		90	<1
18			1	4		83	
19		DMF	11	3		96	2
20			4	3		95	2

[a] Reactions were conducted by stirring 0.35 mmol of geranyl chloride with the metal halide in 300 μL of solvent. Reactions were quenched with cold water, and the allylic halides were recovered by extraction with pentane. [b] Amount present in the recovered mixture of allylic halides. [c] Reaction products were analyzed in benzene solutions by 200-MHz ^{1}H NMR spectroscopy. Doublets arising from the halogen-bearing methylene group in the *Z* chloride, *E* chloride, *Z* bromide, and *E* bromide were observed at δ 3.81, 3.77, 3.71, and 3.67, respectively. In several cases, the extent of isomerization was also determined by GLC analysis of the *E* and *Z* methyl ethers formed by treating the product bromides with NaOMe in MeOH at 25 °C for 4 h.

distillation of commercial dimethyl 3-methylglutaconate, reduction of the more volatile *Z* isomer to diol **17** with AlH_3, and selective replacement of the allylic hydroxyl group by chlorine by using the reagent prepared from dimethyl sulfide and *N*-chlorosuccimide.[11] The conversion of base-sensitive **18** to its trimethylsilyl ether was accomplished by using hexamethyldisilazane (HMDS) and chlorotrimethylsilane.[12] While chloride **19** was reasonably stable, samples completely free of HMDS could not be obtained from small-scale preparations. It is likely that on a larger scale the HMDS could be completely removed by fractional distillation.

Treatment of **2a** with allyllithium readily gave ylide anion **4** ($R_1 = R_2 = H$, $R_3 = C_3H_5$), but this anion could not be successfully alkylated with chloride **19**. Under a variety of reaction conditions, only the product resulting from the protonation of **4** could be isolated. While anion quenching was thought to have been partially a result of HMDS contamination in **19**, the progressive disappearance of **19** from the reaction mixture suggested that dehydrohalogenation of **19** by **4** might be largely responsible for this result. Furthermore, allyl chloride, which lacks the hydrogens required for a 1,4-dehydrochlorination, underwent the desired alkylation reaction, although slowly, requiring several days at 25 °C for completion. The use of prenyl bromide, where 1,4-dehydrohalogenation is again possible, led to very rapid alkylations in model reactions, suggesting that by using the more reactive bromide **20** anion quenching might be avoided. Attempts to prepare **20** from **17** by selective replacement of the allylic hydroxyl group with bromine, by using the dimethyl sulfide–*N*-bromosuccimide method of Corey,[11] were not successful, apparently owing to the ease in which the bromohydrin corresponding to **18** undergoes cyclization to the ether. In light of this failure we turned our attention to the conversion of chloride **19** to bromide **20** by halide ion exchange.

While there has been an excellent study of the conversion of alkyl chlorides to bromides by halide ion exchange,[13] we were unable to find a systematic study of such an exchange with allylic halides.[14] We therefore briefly investigated the conversion of geranyl chloride to its bromide under a variety of conditions as a model for this transformation, and the results of this study are shown in Table III. The use of LiBr in THF (entry 1), suggested by the work of Stotter and Hill,[15] who observed rapid exchange with γ-chlorotiglic acids and esters with no double bond isomerization, is seen to give moderately good exchange (88%) with only slight double bond isomerization when 4-fold excess of LiBr is used over 4 h at 25 °C. The exchange may be driven to near completion by using an 11-fold excess of LiBr but at the expense of an increase in olefin isomerization (entry 2). An increase in the reaction temperature is seen to seriously increase olefin isomerization (entry 3). Similar results were noted in experiments using chloride **19**. The use of LiBr in acetone or acetonitrile is seen to give poorer conversions to the bromide, and NaBr in these solvents resulted in only minor amounts of halide exchange.

Very satisfactory results were obtained by using NaBr in either *N*-methylpyrrolidinone (NMP) or dimethylformamide (DMF), however. In NMP, maximum conversion to the bromide is obtained in 1.5 h at 25 °C with no detectable double bond isomerization when an 11-fold excess of NaBr (entry 12) is used. It is interesting to note that the bromide is still highly favored when lesser amounts of NaBr are employed in this solvent, likely owing to the low solubility of NaCl in NMP.[13] In DMF, a 4-fold excess of NaBr gives 95% of recovered halides as the bromide (entry 20). It would appear that the use of NaBr in either NMP or DMF constitutes a very satisfactory method for the conversion of allylic chlorides to bromides with preserva-

(12) Wellburn, A. R.; Hemming, F. W. *J. Chromatogr.* **1966**, *23*, 51.

(13) Willy, W. E.; McKean, D. R.; Garcia, B. A. *Bull. Soc. Chem. Jpn.* **1976**, *49*, 1989.

(14) Magid, R. M. *Tetrahedron* **1980**, *36*, 1901.

(15) Stotter, P. L.; Hill, K. A. *Tetrahedron Lett.* **1975**, 1679.

tion of stereochemical integrity.

While the desired conversion of chloride **19** to bromide **20** was likewise readily effected with NaBr in NMP, the continuing inability to remove small amounts of protic HMDS led us to instead focus on preparing tetrahydropyranyl-protected bromide **22**. The treatment of chlorohydrin **18** with dihydropyran in acidic dichloromethane gave protected chloride **21** in 74% yield. This derivative was readily purified by distillation, is stable for at least for several weeks at −20 °C, but discolors in several days at 25 °C. Conversion to the bromide **22** was effected with NaBr in NMP in 72% yield. This bromide could also be purified by rapid distillation but was notably less stable than chloride **21**.

Treatment of **2a** with allyllithium and alkylation of the resulting ylide anion with **22** gave the desired functionalized ylide **23** (R = THP) in 87% yield. Decarbalkoxylation was achieved by heating **23** in HOAc at 90 °C for 26 h, giving ylide acetate **24a** in 86% yield after purification by thick-layer chromatography (PTLC). Hydrolysis of the acetate gave ylide alcohol **24b** which was hydrolyzed to ketone **25a** in 84% yield by being heated in aqueous ethanol for 24 h. Acetylation of **25a** with acetic anhydride and pyridine gave the corresponding acetate, **25b**, in 92% yield. Treatment of **25b** with a slight excess of methylenetriphenylphosphorane in THF at 20 °C gave, in addition to a considerable amount of recovered ketone, the desire pheromone **14** in 28% yield (48% based on recovered starting material). The efficiency of this olefination was increased, somewhat, through the use of a 5-fold excess of the Wittig reagent and through the use of more vigerous reaction conditions[16] (1.5 h at 20 °C, 1.5 h at 50 °C), giving, after reacetylation of the reaction product and purification by PTLC, **14** in 47% yield (57% based on recovered starting materials). The 200-MHz ^{1}H NMR spectrum of this material in CS_2 corresponded closely to the reported 300-MHz spectrum of the natural product, and our synthetic sample was found by GLC (6 ft × 0.25 in., 10% UCW-98 column) to correspond to the more mobile isomer in an authentic sample containing a 1:1 mixture of *E* and *Z* isomers.[17] GLC analysis also revealed the presence of only 2% of the *E* isomer, further attesting to the preservation of olefin stereochemical integrity in both the manipulations required for the preparation of alkylating agent **22** as well as those associated with generating the methyl ketone function from functionalized ylide **23**.

In summary, unsaturated ylides **2** serve as excellent methyl vinyl ketone equivalents in conjugate addition–alkylation reactions. Highly substituted methyl ketones **13**, readily prepared as outlined in Scheme II, result from the manipulation of the ylide moiety present in the substituted ylides **6** which arise from the conjugate addition–alkylation process.

Experimental Section

General Methods. Infrared spectra were recorded as films (neat) or as solutions ($CHCl_3$, 0.1 mm) with a Beckman AccuLab 1 spectrometer. ^{1}H NMR spectra were recorded at 60 MHz with a Varian EM 360 spectrometer, at 100 MHz with a JEOL MH-100 spectrometer, or at 200 MHz with a Nicolet NT-200 spectrometer as indicated. Chemical shifts are reported in parts per million (δ) relative to added tetramethylsilane. ^{13}C NMR spectra were recorded at 22.62 MHz with a Bruker WH-90 spectrometer or at 50.31 MHz with a Nicolet NT-200 spectrometer. Preparative thick-layer chromatography (PTLC) was performed on 20 × 20 cm plates coated with a 1–2-mm layer of Merck silica gel 60 PF-254. Baker 60–200-mesh silica powder was used for column chromatography. Bulb-to-bulb distillations of the Kugelrohr type were conducted at the air oven temperatures and pressures cited. Melting points are uncorrected. Analyses were performed by Galbraith Laboratories, Inc.

Alkyllithium reagents (*n*-BuLi in hexane, PhLi in benzene–diethyl ether, and MeLi–LiBr complex in diethyl ether) were obtained from Aldrich Chemical Co. and titrated[18] prior to use. All reactions involving air-sensitive materials were conducted under an argon atmosphere. Reactions said to be conducted at −78 °C employed a dry ice–acetone cooling bath. Tetrahydrofuran (THF) was distilled from sodium-benzophenone ketyl prior to use.

***tert*-Butyl (Triphenylphosphoranylidene)acetate (7).**[15] A solution containing 47.2 g (0.18 mol) of triphenylphosphine and 24.9 g (0.16 mol) of *tert*-butyl chloroacetate[19] in 200 mL of benzene was heated at reflux for 48 h. The phosphonium salt which resulted was collected by filtration and washed with a total of 300 mL of benzene. Drying in air gave 55.1 g (84%) of this salt. The yield of the phosphonium salt could be increased to 95% by reheating the filtrate at reflux for an additional 6 days. A portion of the crude salt (55.1 g, 10.3 mmol) was dissolved in 1 L of water whose temperature was then adjusted to 5 °C by the addition of ice. A cold solution containing 6.0 g (0.15 mol) of NaOH in 200 mL of water was then added with vigorous stirring. The solid which resulted was collected by filtration, washed well with cold water, and air-dried, giving 47.7 g (98%) of **7**: mp 154–155 °C (lit.[15] mp 151–152 °C); IR ($CHCl_3$) 3000, 2980, 1605, 1435, 1360, 1162, 1102 cm^{-1}; ^{1}H NMR ($CDCl_3$, 60 MHz) δ 1.26 (br s, 9 H, CH_3), 2.78 (br d, 1 H, HC=P), 7.2–8.1 (m, 15 H, pH); ^{13}C NMR ($CDCl_3$) δ 28.8 (CH_3), 31.4 (HCP, J_{CP} = 116 Hz), 76.3 (C–O), 128.6 (Ph, $^1J_{CP}$ = 92.7 Hz), 128.6 (Ph, $^2J_{CP}$ = 13.2 Hz), 131.7 (Ph, $^4J_{CP}$ = 2.9 Hz), 133.0 (Ph, $^3J_{CP}$ = 10.3 Hz), 171.0 (C=O).

***tert*-Butyl 3-Oxo-2-(triphenylphosphoranylidene)-4-pentenoate (2a).** A solution containing 7.52 g (20 mmol) of **7** in 50 mL of dry benzene was cooled to 8 °C. 3-Chloropropanoyl chloride (1.27 g, 10 mmol) in 8 mL of dry benzene was added with stirring over 1 min. After stirring for 5 min at 5–10 °C, the mixture was warmed to 25 °C and stirred for an additional 30 min whereupon 60 mL of ether was added to complete the precipitation of the hydrochloride salt of **7**. The salt was removed by filtration, washed with ether, and saved for reuse in the preparation of **7**. The combined filtrates were concentrated under reduced pressure, giving 4.25 g (91%) of crude β-chloroacyl ylide **11** which was used without further purification. (Attempts to purify this intermediate by crystallization or chromatography invariably resulted in its contamination with **2a** as a result of dehydrochlorination). Crude **11** (2.3 g, 5 mmol) was placed in 4 mL of MeOH, treated with 10 mmol of NaOMe in MeOH (approximately 2 N), and stirred at 25 °C until completion of the dehydrochlorination reaction (approximately 1 h) which was conveniently monitored by TLC (4:1 dichloromethane–ethyl acetate). Solvent was carefully removed in vacuo at 15–25 °C, and the residue was quickly treated with 70 mL of water and extracted with dichloromethane. The residue obtained after evaporation of the dried extracts (Na_2SO_4) crystallized from ethyl acetate–hexane, giving 1.60 g (74%) of **2a**: mp 160.5–161.5 °C; IR ($CHCl_3$) 3000, 2980, 1650, 1517, 1330, 1104, 1086 cm^{-1}; ^{1}H NMR ($CDCl_3$, 60 MHz) δ 1.08 (s, 9 H, CH_3), 5.47 (dt, 1 H, C=CH_2, J_{AX} = 10 Hz, J_{AB} = 3.5 Hz, $^4J_{HP}$ = 3.5 Hz), 6.13 (dd, 1 H, C=CH_2, J_{BX} = 17.5 Hz, J_{AB} = 3.5 Hz), 7.4–8.1 (m, 16 H, C=CH_X and aromatic); ^{13}C NMR ($CDCl_3$) δ 29.4 (CH_3), 72.3 (d, C-2, J_{CP} = 108.8 Hz), 78.8 (C–O), 127.0 (d, Ph, $^1J_{CP}$ = 92.7 Hz), 128.5 (d, Ph, $^2J_{CP}$ = 13.2 Hz), 131.4 (d, Ph, $^4J_{CP}$ = 2.9 Hz), 133.0 (d, Ph, $^3J_{CP}$ = 10.3 Hz), 167.0 (d, CO_2, J_{CP} = 13.2 Hz), 186.3 (d, C=O, J_{CP} = 4.3 Hz). Anal. Calcd for $C_{27}H_{27}O_3P$: C, 75.33; H, 6.32. Found: C, 75.33; H, 6.19.

***tert*-Butyl 3-Oxo-2-(triphenylphosphoranylidene)-(*E*)-4-hexenoate (2b).** A solution containing 17.2 g (46 mmol) of **7** in 120 mL of dry benzene was cooled to 8 °C and with vigorous stirring there was added a solution containing 2.15 mL (22 mmol)

(16) (a) Sondheimer, F.; Mechoulam, R. *J. Am. Chem. Soc.* **1958**, *80*, 3087. (b) *Ibid.* **1957**, *79*, 5029.

(17) An authentic sample of (*R*)-**14** as a 1:1 mixture of *E* and *Z* isomers was kindly provided by Dr. Richard Anderson of Zoecon Corp.

(18) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.

(19) Baker, R. H.; Bordwell, F. G. "Organic Syntheses"; Wiley: New York, 1955; Collect. Vol. III, p 141.

of crotonyl chloride in 10 mL of benzene. The mixture was stirred for 10 min at 8–10 °C and then for 30 min at 25 °C whereupon 100 mL of diethyl ether was added and the hydrochloride salt of **7** was removed by filtration. Concentration of the filtrate gave an oil which crystallized from ethyl acetate–hexane, giving 4.1 g (41%) of **2b**: mp 166–167 °C. A second crop may be obtained by chromatographing the filtrate on a short column of silica gel (5:1 dichloromethane–ethyl acetate) followed by crystallization: IR ($CHCl_3$) 3000, 2980, 1650, 1510, 1365, 1165, 1105, 1088 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 1.08 (s, 9 H, CH_3), 1.90 (dd, 3 H, CH_3, $^2J_{HP}$ = 6.5 Hz; $^3J_{HP}$ = 1.5 Hz), 6.4–7.1 (m, 1 H, H-5), 7.3–8.2 (m, 16 H, aromatic and H-4); ^{13}C NMR ($CDCl_3$) δ 17.9 (C-6), 28.1 (CH_3), 71.6 (d, C=P, J_{CP} = 110.3 Hz), 78.5 (C–O), 127.4 (d, Ph, $^1J_{CP}$ = 94.1 Hz), 128.5 (d, Ph, $^2J_{CP}$ = 11.8 Hz), 130.4 (d, C-4, $^3J_{CP}$ = 8.8 Hz), 131.3 (d, Ph, $^4J_{CP}$ = 2.9 Hz), 132.9 (d, Ph, $^3J_{CP}$ = 10.3 Hz), 135.7 (C-5), 167.0 (d, CO_2, $^2J_{CP}$ = 13.2 Hz), 186.6 (d, C=O, $^2J_{CP}$ = 4.4 Hz). Anal. Calcd for $C_{28}H_{29}O_3P$: C, 75.66; H, 6.58. Found: C, 75.82; H, 6.79.

***tert*-Butyl 3-Oxo-5-phenyl-2-(triphenylphosphoranylidene)-(*E*)-4-pentenoate (2c).** In the manner described above for the preparation of **2b**, 7.52 g (20 mmol) of **7** and 1.67 g (10 mmol) of cinnamoyl chloride gave 4.05 g (80%) of **2c**: mp 171–172.5 °C (from ethyl acetate–hexane); IR ($CHCl_3$) 3002, 2980, 1656, 1649, 1630, 1362, 1103, 1085 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.13 (s, 9 H, CH_3), 7.2–8.2 (m, 16 H, Ph and H-5), 8.57 (d, 1 H, H-4, J_{AB} = 16 Hz); ^{13}C NMR ($CDCl_3$) δ 28.2 (CH_3), 73.2 (d, C=P, J_{CP} = 111.8 Hz), 78.8 (C–O), 127.3 (d, PhP, $^1J_{CP}$ = 94.1 Hz), 128.0 (Ph), 128.2 (Ph), 128.4 (Ph), 128.5 (d, PhP, $^2J_{CP}$ = 13.2 Hz), 130.4 (d, C-4, $^3J_{CP}$ = 8.8 Hz), 131.4 (d, PhP, $^4J_{CP}$ = 2.9 Hz), 133.0 (d, PhP, $^3J_{CP}$ = 10.3 Hz), 136.7 and 137.1 (C-5 and Ph). Anal. Calcd for $C_{33}H_{31}O_3P$: C, 78.24; H, 6.17. Found: C, 78.19; H, 6.36.

***tert*-Butyl 3-Oxo-2-(triphenylphosphoranylidene)octanoate (8b).** In the manner described for the preparation of **2b**, 15.04 g (40 mmol) of **7** and 2.69 g (20 mmol) of hexanoyl chloride give 8.3 g (83%) of **8b**: mp 113–114 °C (from hexane–ethyl acetate); IR ($CHCl_3$) 3900, 3970, 3935, 1652, 1540, 1434, 1362, 1305, 1170, 1105, 1080 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 0.87 (t, 3 H, CH_3), 1.10 (s, 9 H, CH_3), 1.0–1.9 (br, 8 H, CH_2), 2.97 (t, 2 H, CH_2C=O, J = 7.5 Hz), 7.4–8.2 (m, 15 H, Ph); ^{13}C NMR ($CDCl_3$) δ 14.1 (C-8), 22.7 (C-7), 25.6 (C-5), 28.1 (CH_3), 31.9 (C-6), 40.0 (d, C-4, $^3J_{CP}$ = 7.3 Hz), 71.1 (d, C-2, $^1J_{CP}$ = 108.8 Hz), 78.2 (C–O), 127.6 (d, Ph, $^1J_{CP}$ = 94.1 Hz), 128.4 (d, Ph, $^2J_{CP}$ = 11.7 Hz), 131.2 (d, Ph, $^4J_{CP}$ = 2.9 Hz), 133.0 (d, Ph, $^3J_{CP}$ = 8.8 Hz), 167.3 (d, C-1, $^2J_{CP}$ = 14.7 Hz), 197.1 (d, C-3, $^2J_{CP}$ = 2.9 Hz). Anal. Calcd for $C_{30}H_{35}O_3P$: C, 75.91; H, 7.45. Found: C, 76.17; H, 7.50.

***tert*-Butyl 4-Methyl-3-oxo-2-(triphenylphosphoranylidene)nonanoate (6a).** A solution containing 431 mg (1.0 mmol) of **2a** in 8 mL of THF was cooled to −78 °C, and 1.3 mL (2.0 mmol) of 1.54 *N* *n*-BuLi solution was added dropwise over several minutes. The dark orange mixture was stirred for 10 min at −78 °C and then for 10 min at 0 °C followed the addition of 125 μL (2.0 mmol) of methyl iodide. The mixture was stirred at 25 °C for 30 min. Solvent was removed under reduced pressure, and the residue was extracted with several small volumes of dichloromethane. Purification of the extract by PTLC (5:1 dichloromethane–ethyl acetate) gave 483 mg (96%) of **6a** as an oil which crystallized from hexane: mp 99–99.5 °C; IR ($CHCl_3$) 2960, 2930, 1655, 1533, 1305, 1168, 1103, 1080 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 0.83 (t, 3 H, CH_2CH_3), 1.12 (s, 9 H, CH_3C), 1.0–1.7 (m, 11 H, CH_2 and 4-CH_3), 3.93 (m, 1 H, CH_3), 7.4–8.2 (m, 15 H, Ph); ^{13}C NMR ($CDCl_3$) δ 14.1 (C-9), 18.2 (4-CH_3), 22.7 (C-8), 27.1 (C-6), 28.1 (CH_3), 32.1 (C-7), 34.1 (C-5), 39.6 (d, C-4, $^3J_{CP}$ = 5.9 Hz), 71.7 (d, C-2, $^1J_{CP}$ = 107.4 Hz), 78.3 (C–O), 127.7 (d, Ph, $^1J_{CP}$ = 94.1 Hz), 128.3 (d, Ph, $^2J_{CP}$ = 11.8 Hz), 131.1 (d, Ph, $^4J_{CP}$ = 2.9 Hz), 132.9 (d, Ph, $^3J_{CP}$ = 10.3 Hz), 167.0 (d, C-1, $^2J_{CP}$ = 14.7 Hz), 200.8 (C-3). Anal. Calcd for $C_{32}H_{39}O_3P$: C, 76.47; H, 7.82. Found: C, 76.52; H, 7.88.

***tert*-Butyl 3-Oxo-4-pentyl-2-(triphenylphosphoranylidene)nonanoate (6b).** Ylide **2a** (431 mg, 1.0 mmol) in 8 mL of THF was treated with 0.78 mL (1.2 mmol) of 1.54 N *n*-BuLi solution at −78 °C. After being stirred for 10 min, the dark orange solution was treated with 175 μL (1.34 mmol) of *n*-amyl iodide, allowed to warm to 25 °C, and stirred at this temperature for 3 h. Solvent was removed under reduced pressure, and the residue was chromatographed (PTLC, 15:1 dichloromethane–ethyl acetate), giving 464 mg (83%) of **6b** as an oil which crystallized from hexane: mp 71–72 °C; IR ($CHCl_3$) 2955, 2920, 1650, 1530, 1430, 1108, 1157 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 0.83 (t, 6 H, CH_3), 1.10 (s, 9 H, CH_3), 1.0–1.7 (br, 16 H, CH_2), 3.87 (br, 1 H, CH), 7.3–8.1 (m, 15 H, Ph); ^{13}C NMR ($CDCl_3$) δ 14.1 (C-9), 22.7 (C-8), 27.0 (C-6), 28.1 (CH_3), 32.3 (C-7), 33.1 (C-5), 44.3 (d, C-4, $^3J_{CP}$ = 5.9 Hz), 73.7 (d, C-2, $^1J_{CP}$ = 107.4 Hz), 78.3 (OCH_3), 127.8 (d, Ph, $^1J_{CP}$ = 92.6 Hz), 128.3 (d, Ph, $^2J_{CP}$ = 11.8 Hz), 131.1 (d, Ph, $^4J_{CP}$ = 2.9 Hz), 132.9 (d, Ph, $^3J_{CP}$ = 10.3 Hz), 167.0 (d, C-1, $^2J_{CP}$ = 14.8 Hz), 199.9 (d, C-3, $^2J_{CP}$ = 2.9 Hz). Anal. Calcd for $C_{36}H_{47}O_3P$: C, 77.39; H, 8.48. Found: C, 77.23; H, 8.61.

***tert*-Butyl 5-(1,3-Dithian-2-yl)-4-methyl-3-oxo-2-(triphenylphosphoranylidene)pentanoate (6c).** A solution of 2-lithio-1,3-dithiane[20] was prepared by treating 960 mg (8.0 mmol) of 1,3-dithiane in 12 mL of THF with 5.1 mL (8.0 mmol) of 1.57 N *n*-BuLi solution at −30 °C for 1.5 h. To this stirred solution was added dropwise by cannula a solution containing 1.72 g (4.0 mmol) of **2a** in 6 mL of THF. The resulting dark brown mixture was stirred for 10 min at −30 °C and then treated with 935 μL (15.0 mmol) of ethyl iodide. The mixture was warmed to 25 °C and allowed to stand for 15 min whereupon it was poured into 75 mL of water and extracted with 500 mL of 1:1 dichloromethane–diethyl ether. The organic phase was dried over Na_2SO_4, and the residue obtained upon removal of the solvent was dissolved in dichloromethane and passed through a short column of silica gel. Solvent removal gave 1.90 g (84%) of nearly pure **6c** as an oil. Further purification by PTLC (5:1 dichloromethane–ethyl acetate) gave crystalline **6c**: mp 133–133.5 °C (from ethyl acetate–hexane); IR ($CHCl_3$) 3000, 2980, 1655, 1532, 1438, 1310, 1168, 1105, 1088 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 1.12 (s, 9 H, CH_3), 1.0–1.3 (d, 3 H, 4-CH_3), 1.7–2.4 (br, 2 H, dithiane, 5-CH_2), 2.4–3.1 (br m, 4 H, CH_2S), 3.5–4.5 (m, 2 H, HCS and 4-H), 7.4–8.2 (m, 15 H, Ph); ^{13}C NMR ($CDCl_3$) δ 18.7 (4-CH_3), 26.2 (dithiane CH_2), 28.2 (CH_3), 29.7 (dithiane CH_2), 37.5 (d, C-4, $^3J_{CP}$ = 7.3 Hz), 38.7 (C-5), 45.3 (dithiane CH), 71.7 (d, C-2, $^1J_{CP}$ = 107.4 Hz), 78.5 (C–O), 127.5 (d, Ph, $^1J_{CP}$ = 92.6 Hz), 128.3 (d, Ph, $^2J_{CP}$ = 13.2 Hz), 131.2 (d, Ph, $^4J_{CP}$ = 2.9 Hz), 132.9 (d, Ph, $^3J_{CP}$ = 10.3 Hz), 166.8 (d, C-1, $^2J_{CP}$ = 14.7 Hz), 198.4 (C-3). Anal. Calcd for $C_{32}H_{37}O_3PS_2$: C, 68.06; H, 6.60. Found: C, 68.03; H, 6.72.

***tert*-Butyl 3-Oxo-5-phenyl-2-(triphenylphosphoranylidene)pentanoate (6d).** A solution containing 431 mg (1.0 mmol) of **2a** in 8 mL of THF was cooled to −78 °C and with stirring was treated with 2.0 mL (1.2 mmol) of a 0.6 N PhLi solution. The dark orange solution was stirred at −78 °C for 20 min and then at 0 °C for 5 min whereupon 60 μL of water was added. Solvents were removed in vacuo, and the residue was extracted with dichloromethane and purified by PTLC (5:1 dichloromethane–ethyl acetate), giving 379 mg (75%) of **6d**: mp 164–165 °C (from ethyl acetate–hexane); IR ($CDCl_3$) 3000, 1652, 1542, 1438, 1361, 1304, 1163, 1103, 1082 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 1.07 (s, 9 H, CH_3), 2.8–3.6 (m, 4 H, CH_2), 7.1–8.1 (m, 15 H, Ph); ^{13}C NMR ($CDCl_3$) δ 28.1 (CH_3), 31.7 (C-5), 41.0 (d, C-4, $^3J_{PC}$ = 4.3 Hz), 71.2 (d, C-2, $^1J_{CP}$ = 107.4 Hz), 78.3 (C–O), 125.3, 128.0, 128.7, 142.8 (Ph), 127.3 (d, PhP, $^1J_{CP}$ = 92.6 Hz), 128.4 (d, PhP, $^2J_{CP}$ = 13.2 Hz), 131.4 (d, PhP, $^4J_{CP}$ = 2.9 Hz), 133.0 (d, PhP $^3J_{CP}$ = 8.8 Hz). Anal. Calcd for $C_{33}H_{33}O_3P$: C, 77.93; H, 6.54. Found: C, 77.76; H, 6.62.

This compound was also prepared from **7** and hydrocinnamoyl chloride in 94% yield by using the procedure described above for the preparation of **2b**.

***tert*-Butyl 3-Oxo-5-phenyl-4-propyl-2-(triphenylphosphoranylidene)pentanoate (6e).** To a stirred solution of **2a** (1.72 g, 4.0 mmol) in 20 mL of THF was added dropwise at −78 °C 2.6 mL (4.8 mmol) of a 1.85 N PhLi solution. The mixture was stirred for 15 min at 78 °C and then for 10 min at 0 °C whereupon *n*-propyl iodide (505 μL, 5.2 mmol) was added and stirring was continued at 25 °C for 2.5 h. Solvent was removed under reduced pressure followed by the addition of water and dichloromethane. The organic extract was dried over Na_2SO_4 and then concentrated, giving **6e** as an oil which crystallized; 2.15 g (98%). An analytical sample was obtained after PTLC (5:1 dichloromethane–ethyl acetate) and recrystallization from ethyl acetate–hexane: mp 125–126 °C; IR ($CHCl_3$) 3002, 2970, 2935,

(20) Corey, E. J.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 1075.

1655, 1435, 1440, 1392, 1365, 1310, 1170, 1105, 1082 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 0.90 (t, 3 H, CH_3), 1.07 (s, 9 H, CH_3), 1.2–1.7 (br, 4 H, CH_2), 2.3–3.4 (m, 2 H, $PhCH_2$), 4.25–4.70 (br, 1 H, CH), 7.40 (s, 5 H, Ph), 7.2–8.0 (m, 15 H, PhP); ^{13}C NMR ($CDCl_3$) δ 14.5 (CH_3), 20.5 (CH_2), 28.1 (CH_3), 35.3 (CH_2), 28.8 (C-5), 45.4 (d, C-4, $^3J_{CP}$ = 5.9 Hz), 73.3 (d, C-2, $^1J_{CP}$ = 107.4 Hz), 78.2 (C–O), Ph at 125.1, 127.8, 129.4, and 141.6, PhP at 127.5 (d, $^1J_{CP}$ = 94.1 Hz), 128.3 (d, $^2J_{CP}$ = 13.2 Hz), 131.1 (d, $^4J_{CP}$ = 2.9 Hz), 132.9 (d, $^3J_{CP}$ = 10.3 Hz), 166.7 (d, C-1, $^2J_{CP}$ = 14.7 Hz), and 198.7 (d, C-3, $^2J_{CP}$ = 2.9 Hz). Anal. Calcd for $C_{36}H_{39}O_3P$: C, 78.52; H, 7.14. Found: C, 78.79; H, 7.13.

***tert*-Butyl 4-Benzyl-3-oxo-5-phenyl-2-(triphenylphosphoranylidene)hexanoate (6f).** A solution containing 889 mg (2.0 mmol) of **2b** in 12 mL of THF was cooled to −78 °C, and 1.3 mL (2.4 mmol) of a 1.85 N PhLi solution was added dropwise with stirring. After 15 min at −78 °C stirring was continued at 0 °C for 10 min, and 309 μL (2.6 mmol) of benzyl bromide was added. The mixture was allowed to stand at 25 °C for 5 h, treated with 80 mL of water, and extacted with several portions of dichloromethane. Concentration of the dried extract (Na_2SO_4) gave an oil which upon crystallization from ethyl acetate afforded 1.02 g (84%) of **6f**. An analytical sample had the following: mp 199.5–204 °C; IR ($CHCl_3$) 3005, 3975, 1658, 1438, 1380, 1300, 1178, 1105, 1080 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 1.05 (s, 9 H, CH_3), 1.45 (d, 3 H, CH_3, J = 7 Hz), 2.3–3.2, (m, 3 H, benzylic), 4.75–5.35 (m, 1 H, CH), 7.32 (s, 10 H, Ph), 7.1–7.9 (m, 15 H, PhP); ^{13}C NMR ($CDCl_3$) δ 20.7 (C-6), 28.1 (CH_3), 37.9 ($PhCH_2$), 44.3 (C-5), 50.2 (C-4), 75.1 (d, C-2, $^1J_{CP}$ = 107.4 Hz), 78.4 (C–O), Ph at 125.7, 127.6, 128.2, 141.5, and 147.1, PPh at 127.1 (d, $^1J_{CP}$ = 98.5 Hz), 128.2 (d, $^2J_{CP}$ = 13.2 Hz), 131.1 (d, $^4J_{CP}$ = 2.9 Hz), 132.9 (d, $^3J_{CP}$ = 10.3 Hz), 166.6 (d, C-1, $^2J_{CP}$ = 13.2 Hz), and 197.5 (C-3). Anal. Calcd for $C_{41}H_{41}O_3P$: C, 80.37; H, 6.74. Found: C, 80.45; H, 7.05.

By use of a similar procedure, **6f** was also prepared by the addition of 4.8 mmol of MeLi to 4.0 mmol of **2c** in THF (−78 °C, 0.5 h; 0 °C, 8 min) followed by alkylation with 5.2 mmol of benzyl bromide (25 °C, 1.25 h). Extraction gave 2.53 g (99%) of crude **6f** which was identical with material from the first preparation.

***tert*-Butyl 4-Benzyl-5-methyl-3-oxo-2-(triphenylphosphoranylidene)nonanoate (6g).** To a solution containing 659 mg (1.48 mmol) of **2b** in 10 mL of THF was added with stirring at −78 °C 1.13 mL (1.8 mmol) of a 1.57 N *n*-BuLi solution over 2 min. The dark orange solution was stirred at −78 °C for 10 min and then at 0 °C for 10 min whereupon 230 μL (1.93 mmol) of benzyl bromide was added. After 2 h at 25 °C, water (80 mL) was added, and the mixture was extracted with four portions of dichloromethane which were then dried over Na_2SO_4. Evaporation gave 857 mg (98%) of crude **6g** of sufficient purity for subsequent use. An analytical sample was obtained by PTLC (5:1 dichloromethane–ethyl acetate) and crystallization from ethyl acetate–hexane: mp 99–103.5 °C; IR ($CHCl_3$) 2970, 2940, 1658, 1533, 1438, 1300, 1170, 1108, 1085 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.8–1.1 (m, 6 H, CH_3), 1.05 (s, 9 H, CH_3), 1.0–2.0 (br, 7 H, CH_2 and 5-H), 2.6–3.1 (m, 2 H, benzylic CH_2), 4.20–4.75 (m, 1 H, 4-H), 7.40 (s, 5 H, Ph), 7.1–7.9 (m, 15 H, Ph); ^{13}C NMR ($CDCl_3$) δ 14.3 (C-9), 17.5 (5-CH_3), 23.1 (C-8), 28.1 (CH_3), 29.8 (C-7), 33.0 (C-6), 34.6 (C-5), 36.5 (benzylic C), 50.1 (d, C-4, $^3J_{CP}$ = 5.9 Hz), 74.3 (d, $^1J_{CP}$ = 107.4 Hz), 78.2 (C–O), Ph at 125.0, 127.8, 128.5, and 142.2, PhP at 127.4 (d, $^1J_{CP}$ = 91.2 Hz), 128.2 (d, $^2J_{CP}$ = 11.8 Hz), 131.0, 132.9 (d, $^3J_{CP}$ = 10.3 Hz), 166.5 (d, C-1, $^2J_{CP}$ = 11.8 Hz), and 197.9 (C-3). Anal. Calcd for $C_{39}H_{45}O_3P$: C, 79.03; H, 7.65. Found: C, 79.07; H, 7.81.

***tert*-Butyl 4-Methyl-3-oxo-5-phenyl-2-(triphenylphosphoranylidene)nonanoate (6h).** To a −78 °C solution containing 1.02 g (2.0 mmol) of **2c** in 12 mL of THF was added dropwise with stirring 1.53 mL (2.4 mmol) of a 1.57 N BuLi solution. The dark mixture was stirred for 1 min at −78 °C and then for 10 min at 0 °C whereupon 164 μL (2.6 mmol) of methyl iodide was added. After the mixture had stirred at 25 °C for 1 h, 80 mL of water was added, and the mixture was extracted with several portions of dichloromethane. The dried extracts (Na_2SO_4) gave 1.14 g (98%) of crude crystalline **6h** upon removal of the solvent. This material was of sufficient purity for direct subsequent use. An analytical sample was obtained by PTLC (10:1 dichloromethane–ethyl acetate) and crystallization from ethyl acetate–hexane: mp 155–161.5 °C; IR ($CHCl_3$) 2970, 2938, 1653, 1532, 1432, 1385, 1297, 1164, 1102, 1080 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 0.73 (t, 3 H, CH_3CH_2), 0.80 (d, 3 H, 4-CH_3, J = 8 Hz), 1.12 (s, 9 H, CH_3), 1.0–1.7 (br m, 6 H, CH_2), 2.35–2.90 (br m, 1 H, 5-H), 3.75–4.30 (br m, 1 H, 4-H), 7.20 (s, 5 H, Ph), 7.1–8.0 (br m, 15 H, Ph); ^{13}C NMR ($CDCl_3$) δ 14.0 (C-9), 17.4 (4-CH_3), 22.6 (C-8), 28.2 (CH_3), 29.6 (C-6), 34.2 (C-7), 45.0 (d, C-4, $^3J_{CP}$ = 5.9 Hz), 49.2 (C-5), 73.2 (d, C-2, $^1J_{CP}$ = 107.4 Hz), 78.5 (C–O), 5-Ph at 125.5, 127.9, 128.1, and 133.1, PhP at 124.6 (d, $^1J_{CP}$ = 92.7 Hz), 128.4 (d, $^2J_{CP}$ = 11.8 Hz), 131.2 (d, $^4J_{CP}$ = 2.9 Hz), 132.9 (d, $^3J_{CP}$ = 8.8 Hz), 167.0 (d, C-1, $^2J_{CP}$ = 14.7 Hz), and 199.9 (C-3).

Conversion of Ylides 6 to Ketones 13 (Table II). Typical Procedures. Method A. Ylide **6h** (579 mg, 1.0 mmol) was dissolved in 6 mL of TFA and heated for 1 h in a stoppered flask in an oil bath maintained at 50 °C. Volatiles were removed under reduced pressure, and the residue was concentrated three times again after the addition of 6-mL portions of benzene. The oil which remained was dissolved in 3 mL of ethanol and treated with water until the cloud point was reached (approximately 2 mL). The pH of the mixture was adjusted to 8–10 by the addition of aqueous NaOH, and the mixture was heated on a steam bath for 42 h. The mixture was cooled to 25 °C, treated with 15 mL of brine, and extracted with five 12-mL portions of pentane. The residue obtained after removal of the pentane gave, after bulb-to-bulb distillation (180 °C, 12 mm), 198 mg (91%) of 3-methyl-4-phenyl-2-octanone (**13h**) as a mixture of diastereoisomers: IR (neat) 1710 cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 0.80 (br t, 3 H, CH_3), 1.13 (br d, 3 H, 3-CH_3), 1.2–1.9 (br, 6 H, CH_2), 1.73, 2.13 (s, 3 H, diastereoisomeric $COCH_3$), 2.70 (br m, 2 H, CH), 7.30 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 14.1, 16.2, 17.5, 22.9, 29.2, 29.6, 31.2, 32.1, 33.2, 33.5, 34.9, 35.1, 35.3, 59.9, 60.2, 126.0, 128.4, 128.8, 140.4, 140.7, 211.7, 212.2. Anal. Calcd for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.68; H, 10.11.

While the triphenylphosphine oxide also produced in the hydrolysis is largely excluded by the pentane extraction, small amounts occasionally codistill with less volatile ketones. Chromatography on silica gel (dichloromethane) prior to distillation was used to remove residual triphenylphosphine oxide in those cases.

Method B. A solution of **6c** (741 mg, 1.31 mmol) in 12 mL of glacial HOAc was heated for 30 h in an oil bath maintained at 90 °C. The residue obtained after removal of the HOAc under reduced pressure was reconcentrated four times from solutions obtained by adding 10-mL portions of benzene to the concentrate. The remaining oil was dissolved in 4 mL of ethanol and treated with water until the cloud point was reached (approximately 2 mL). The pH of the mixture was adjusted to 10 by the addition of aqueous NaOH whereupon the mixture was heated on a steam bath for 22 h. The mixture was poured into 15 mL of brine and extracted six times with 10-mL portions of pentane and three times with 10-mL portions of ether. The combined extracts were concentrated, and the residue gave upon bulb-to-bulb distillation (190 °C, 12 mm) 173 mg (65%) of 4-(1,3-dithian-2-yl)-3-methyl-2-butanone (**13c**): IR (neat) 1708 cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 1.12 (d, 3 H, 3-CH_2, J = 6.5 Hz), 1.3–2.2 (m, 4 H, CH_2), 2.17 (s, 3 H, CH_3CO), 2.2–2.6 (m, 1 H, CH), 2.7–3.0 (m, 4 H, CH_2S), 3.97 (t, 1 H, dithiane 5-CH_2, J = 8 Hz); ^{13}C NMR ($CDCl_3$) δ 16.9, 25.9, 28.6, 30.0, 37.7, 43.7, 45.1, 211.0. Anal. Calcd for $C_9H_{16}OS_2$: C, 52.90; H, 7.89. Found: C, 52.91; H, 8.09.

Data for the remaining new ketones found in Table III are listed below.

13b: IR (neat) 1710 cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 0.90 (t, 3 H, CH_3), 1.1–1.9 (br, 16 H, CH_2), 2.07 (s, 3 H, CH_3CO), 2.1–2.5 (m, 1 H, CH); ^{13}C NMR ($CDCl_3$) δ 14.0, 22.5, 27.2, 28.6, 31.7, 32.0, 50.4, 213.0. Anal. Calcd for $C_{13}H_{26}O$: C, 68.72; H, 13.21. Found: C, 78.68; H, 13.16.

13e: IR (neat) 1706 cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 0.90 (br t, 3 H, CH_3), 1.14–1.74 (br m, 4 H, CH_2), 1.95 (s, 3 H, CH_3CO), 2.45–3.05 (m, 3 H, benzylic and CH), 7.33 (br s, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 14.1, 20.6, 30.1, 34.0, 38.0, 54.6, 126.3, 128.5, 128.9, 139.7, 212.1. Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 82.11; H, 9.35.

13f: IR (neat) 1703 cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 1.23 (d, 3 H, CH_3), 1.73 (s, 3 H, CH_3CO), 2.1–2.8 (m, 1 H, CHCO), 2.8–3.3 (m, 3 H, CH_2 and benzylic CH), 6.9–7.6 (m, 10 H, Ph); ^{13}C NMR ($CDCl_3$) δ 18.6, 20.2, 32.4, 33.0, 36.0, 38.0, 42.2, 42.9, 61.6, 62.1, 126.2, 126.5, 126.7, 127.4, 128.4, 128.6, 131.9, 139.6, 144.7, 212.1, 212.9 (a 2:1 mixture of diastereoisomers). Anal. Calcd for $C_{18}H_{20}O$:

C, 85.67; H, 7.99. Found: C, 85.83; H, 8.10.

13g: IR (neat) 1707 cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 1.00 (m, 6 H, CH_3), 1.35–1.75 (m, 6 H, CH_2), 2.05 (2 s, 3 H, CH_3CO), 1.9–2.7 (br m, 2 H, CH), 3.0 (m, 2 H, benzylic), 7.50 (br s, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 14.1, 16.2, 17.5, 22.9, 29.2, 29.6, 31.2, 32.1, 33.2, 33.5, 34.9, 35.1, 35.3, 59.9, 60.2, 126.0, 128.4, 128.8, 140.4, 140.7, 211.7, 212.2 (a 1:1 mixture of diastereoisomers). Anal. Calcd for $C_{16}H_{24}O$: C, 82.70; H, 10.41. Found: C, 82.77; H, 10.52.

(*Z*)-5-Chloro-3-methyl-3-penten-1-ol Trimethylsilyl Ether (19). This compound has been reported[11] as having been previously prepared by the method of Wellburn and Hemming,[12] but experimental details were not provided. A solution containing 700 mg (5.2 mmol) of freshly prepared chlorohydrin **17**[11] and 7.5 mL of chlorotrimethylsilane in 9.0 mL of THF was treated dropwise while stirring with 9.6 mL of hexamethyldisilazane (HMDS). After a brief period of stirring, the mixture was allowed to sit overnight in a closed container whereupon the volatiles were removed at a temperature not exceeding 30 °C under reduced pressure (15 mm). The residue was dissolved in hexane and filtered through a short plug of Celite, and the filtrate was again concentrated in vacuo. The residue was dissolved in 20 mL of pentane, washed with three 10-mL portions of pH 6 buffer and then with brine. The solution was dried briefly over Na_2SO_4, and the solvent was removed under reduced pressure. Bulb-to-bulb distillation of the residue (120 °C, 15 mm) gave 800 mg (74%) of **19** as a clear liquid: IR (neat) 2970, 1665, 1250, 1097, 840 cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 1.77 (br s, 3 H, 3-CH_3), 2.27 (t, 2 H, allylic CH_2, J = 6 Hz), 3.58 (t, 2 H, CH_2O, J = 6.5 Hz), 3.97 (d, 2 H, CH_2Cl, J = 8 Hz), 5.43 (t, 1 H, vinyl H, J = 7 Hz). Chloride **19** slowly decomposes when stored at 25 °C but is stable for several weeks at −20 °C. The presence of HMDS not removed in the workup is evidenced by a singlet at δ 0.07 in NMR spectra.

(*Z*)-5-Chloro-3-methyl-3-penten-1-ol Tetrahydropyranyl Ether (21). A solution containing 1.40 g (10.4 mmol) of freshly prepared chlorohydrin **18**[11] and 5.0 mL of dihydropyran (freshly distilled from KOH) in 15 mL of dichloromethane was treated with approximately 10 mL of vapor taken from a closed container of concentrated hydrochloric acid. The solution was stirred at 25 °C for 1.5 h and then stirred for 10 min with approximately 0.5 g of powdered $NaHCO_3$ followed by the addition of 10 drops of pyridine, added to aid in the removal (by cyclization) of any remaining alcohol **18**. The mixture was treated with 20 mL of water, and the organic phase was washed successively with six 20-mL portions of water and 20 mL of brine and dried over Na_2SO_4. Evaporation of the solvent at 25 °C (15 mm) gave an oil which upon rapid bulb-to-bulb distillation (160 °C, 0.5 mm) gave 1.68 g (74%) of **21**: IR (neat) 2950, 2880, 1665, 1457, 1444, 1356, 1260, 1202, 1148, 1121, 1080, 1032 cm^{-1} NMR (CCl_4, 100 MHz) δ 1.4–2.1 (m, 6 H, CH_2 in THP), 1.86 (s, 3 H, vinyl CH_3), 2.36 (t, 2 H, CH_2CH_2O, J = 7 Hz), 3.32–3.64 (m, 2 H, homoallylic CH_2), 3.64–3.96 (m, 2 H, CH_2O in THP), 4.10 (d, 2 H, CH_2Cl, J = 8 Hz), 4.60 (br s, 1 H, OCHO), 5.56 (t, 1 H, vinyl, J = 8 Hz).

Distilled chloride **21** was either used immediately or stored at −20 °C where no decomposition was noted after several weeks. Samples stored at room temperature slowly discolor.

(*Z*)-5-Bromo-3-methyl-3-penten-1-ol Tetrahydropyranyl Ether (22). A mixture of 3.5 g (34 mmol) of finely ground NaBr and 3.5 mL of 1-methyl-2-pyrrolidinone (NMP) was briefly heated on a steam bath and then cooled to 25 °C. To this mixture was added with magnetic stirring 440 mg (2.0 mmol) of **21**, and stirring was continued during 3 h. The vigorously stirred mixture was treated with 6 mL of pentane followed by 15 mL of cold water, and the pentane layer was separated and washed with six 20-mL portions of water. The combined extracts were dried briefly over Na_2SO_4 and concentrated under reduced pressure at 20 °C. The resulting oil was purified by rapid bulb-to-bulb distillation (170 °C, 0.5 mm), giving 380 mg (72%) of **22** as a colorless oil: NMR (CCl_4, 100 MHz) δ 1.32–2.12 (m, 6 H, CH_2 in THP), 1.81 (s, 3 H, vinyl CH_3), 2.37 (t, 2 H, CH_2CH_2O, J = 7 Hz), 3.20–3.52 (m, 2 H, CH_2OTHP), 3.52–4.06 (m, 2 H, CH_2O in THP), 3.93 (d, 2 H, CH_2Br, J = 8 Hz), 4.49 (br s, 1 H, OCHO), 5.53 (t, 1 H, vinyl, J = 8 Hz).

Bromide 22 is moderately stable at −20 °C over several days but darkens within 1 day at 25 °C.

***tert*-Butyl 4-(3-Buten-1-yl)-7-methyl-3-oxo-9-[(tetrahydro-2*H*-pyran-2-yl)oxy]-2-(triphenylphosphoranylidene)-(*Z*)-6-nonenoate (23, R = THP).** To 235 μL (0.97 mmol) of tetraallyltin was added 2.0 mL (3.0 mmol) of 1.50 N *n*-BuLi in hexane.[21] The mixture was stirred under argon for 3 h, and the thick white suspension which resulted was treated with 5 mL of THF, giving a yellow homogeneous solution of allyllithium which was immediately transferred by cannula over 2 min to a stirred solution containing 903 mg (2.1 mmol) of **2a** in 15 mL of THF cooled to −78 °C. The resulting dark maroon solution was stirred at −78 °C for 15 min and then at 0 °C for 15 min whereupon a solution containing 690 mg (2.6 mmol) of **22** in 7 mL of THF was added by cannula over 2 min. The reaction mixture immediately became lighter in color and was warmed to 27 °C where stirring was continued for 1 h. The mixture was concentrated under reduced pressure, treated with water, and twice extracted with dichloromethane. The extracts were washed twice with water, dried over Na_2SO_4, and concentrated under reduced pressure. The resulting residue was purified by PTLC (5:1 dichloromethane–ethyl acetate, R_f 0.33), giving 1.19 g (87%) of **23** (R = THP) as a thick oil: IR ($CHCl_3$) 1654, 1532, 1438, 1312, 1106, 1082 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 1.10 (s, 3 H, CH_3), 1.2–2.0 (m, 8 H, CH_2), 2.0–2.5 (m, 6 H, allylic CH_2), 3.2–3.6 (m, 2 H, CH_2O in THP), 3.6–4.1 (m, 3 H, CH and homoallylic CH_2O), 4.52 (br s, 1 H, OCHO), 4.7–5.1 (m, 2 H, C=CH_2), 5.22 (t, 1 H, C-6 vinyl H, J = 7 Hz), 5.5–6.0 (m, 1 H, C=CH), 7.2–8.2 (m, 15 H, aromatic).

8-Acetoxy-3-(3-buten-1-yl)-6-methyl-1-(triphenylphosphoranylidene)-(*Z*)-5-octen-2-one (24a). A solution containing 325 mg (0.50 mmol) of **23** (R = THP) in 4 mL of glacial acetic acid was heated at 90 °C under argon for 26 h. The solution was cooled to 25 °C, treated with 2 mL of water, and allowed to stand for 5 h. The volatiles were removed under reduced pressure at 40 °C, and the residue was again concentrated from benzene solution in like manner. The resulting residue was dissolved in dichloromethane, washed successively with water, $NaHCO_3$ solution, water, and brine, and the solvent was removed under reduced pressure after drying over Na_2SO_4. Chromatography (PTLC, 30:1 ethyl acetate–methanol, R_f 0.38) gave 218 mg (86%) of **24a** as a very viscous oil: NMR ($CDCl_3$, 100 MHz) δ 1.2–1.8 (m, 2 H, homoallylic CH_2), 1.74 (s, 3 H, vinyl CH_3), 2.01 (s, 3 H, CH_3CO), 2.0–2.6 (m, 6 H, allylic CH_2), 3.4–4.0 (br m, 1 H, PCH), 4.11 (t, 2 H, CH_2O), 4.0–4.2 (br m, 1 H, CH), 4.8–5.2 (m, 2 H, CH_2=CH), 5.42 (t, 1 H, C-5 vinyl H, J = 6 Hz), 5.6–6.1 (m, 1 H, CH_2=$CHCH_2$), 7.3–8.1 (m, 15 H, aromatic).

3-(3-Butenyl)-8-hydroxy-6-methyl-(*Z*)-5-octen-2-one (25a). A solution containing 470 mg (0.92 mmol) of **24a** and 100 mg of K_2CO_3 in 7 mL of MeOH was stirred at 25 °C for 0.5 h and then concentrated under reduced pressure. The residue was treated with 5 mL of water and twice extracted with 7-mL portions of dichloromethane which were combined and dried over Na_2SO_4. Solvent removal gave 417 mg (97%) of crude alcohol **24b** (TLC, 20:1 ethyl acetate–methanol, R_f 0.23). The crude alcohol (**24b**) was dissolved in 6 mL of EtOH and treated with water until the solution just became cloudy (approximately 3 mL). Several drops of dilute NaOH solution were added, and the resulting pH 9–10 solution was heated on a steam bath for 24 h. Ethanol was removed at 25 °C under reduced pressure, and the aqueous mixture was treated with 7 mL of brine and twice extracted with 10-mL portions of diethyl ether. The extracts were dried over Na_2SO_4, and the oil remaining after evaporation of the solvent gave, upon chromatography (PTLC, 20:1 ethyl acetate–methanol, R_f 0.58), 157 mg (84%) of **25a** as an oil. An analytical sample was obtained by bulb-to-bulb distillation (165 °C, 0.7 mm): IR (neat) 3440, 2970, 1710, 1643, 1450, 1357, 1170, 1045, 912 cm^{-1}; NMR (CCl_4, 200 MHz) δ 1.23–1.56 (m, 2 H, homoallylic CH_2), 1.70 (s, 3 H, vinyl CH_3), 1.92–2.40 (m, 6 H, allylic CH_2), 2.06 (s, 3 H, CH_3CO), 2.40–2.57 (m, 1 H, CH), 3.57 (t, 2 H, CH_2O, J = 6 Hz), 4.90–5.06 (m, 2 H, CH_2=CH), 5.11 (t, 1 H, C-5 vinyl H, J = 7 Hz), 5.60–5.80 (m, 1 H, CH_2=$CHCH_2$). Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.06; H, 10.67.

8-Acetoxy-3-(3-butenyl)-6-methyl-(*Z*)-5-octen-2-one (25b). A mixture containing 107 mg (0.51 mmol) of **25a**, 127 μL of pyridine, and 290 μL of acetic anhydride was allowed to sit at 25 °C for 35 min. Water (250 μL) was added with stirring over several minutes followed by the addition of 7 mL of water. The

(21) Seyferth, D.; Weiner, M. *J. Org. Chem.* **1961**, *26*, 4797.

mixture was extracted with two 10-mL portions of pentane which were combined, washed with water, dilute $NaHCO_3$, dilute hydrochloric acid, and water, and dried over Na_2SO_4. Concentration gave an oil which was purified by PTLC (13:1 dichloromethane–ethyl acetate). Bulb-to-bulb distillation (160 °C, 0.75 mm) afforded 118 mg (92%) of **25b** as an oil: IR (neat) 3080, 2983, 2962, 2930, 1732, 1707, 1640, 1450, 1362, 1230, 1040, 910 cm^{-1}; ^1H NMR (CCl_4, 100 MHz) δ 1.2–1.6 (rı, 2 H, homoallylic CH_2), 1.72 (s, 3 H, vinyl CH_3), 1.99 (s, 3 H, $OCOCH_3$), 2.08 (s, 3 H, CH_3CO), 1.9–2.6 (m, 6 H, allylic CH_2), 4.00 (t, 2 H, CH_2O, J = 7 Hz), 4.84–5.08 (m, 2 H, C=CH_2), 5.10 (t, 1 H, C-5 vinyl H, J = 7 Hz) 5.4–5.9 (m, 1 H, vinyl H).

(±)-(*Z*)-3-Methyl-6-isopropenyl-3,9-decadien-1-ol Acetate (14). A solution of methylenetriphenylphosphorane was prepared by treating 160 mg (0.45 mmol) of methyltriphenylphosphonium bromide in 2 mL of THF with 0.28 mL (0.42 mmol) of 1.50 N *n*-BuLi in hexane at 0 °C followed by stirring for 10 min at 0 °C and then for 15 min at 25 °C. This solution was added dropwise over 2 min by cannula to a stirred solution containing 88 mg (0.35 mmol) of **25b** in 2.5 mL of THF under argon. The mixture was stirred for 0.5 h, and the solvent was removed in vacuo at 25 °C. The residue was treated with 5 mL of water and twice extracted with 5-mL portions of diethyl ether which were combined and then washed with water and dried over Na_2SO_4. The oil obtained after removal of the solvent by distillation was treated with 290 μL (3.1 mmol) of Ac_2O and 125 μL (1.6 mmol) of pyridine and allowed to stand for 0.5 h at 25 °C. Water (250 μL) was added dropwise to the mixture over several minutes followed by treatment with 7 mL of water and extraction with two 10-mL portions of pentane. The combined extracts were successively washed with small portions of aqueous $NaHCO_3$, dilute hydrochloric acid, water, and brine. The residue obtained upon removal of the solvent was chromatographed (PTLC, dichloromethane), giving 17 mg of recovered **25b** and 47 mg (57% based on recovered starting material) of pure (±)-14: IR (neat) 3080, 2970, 2930, 2860, 1734, 1640, 1450, 1362, 1230, 1036, 905, 885 cm^{-1} (the spectrum was nearly identical to that of an authentic sample[17] of a 1:1 moisture of *E* and *Z* isomers); ^1H NMR (CS_2, 200 MHz) δ 1.29–1.45 (m, 2 H, homoallylic CH_2), 1.568, 1.575 (dd, 3 H, isopropenyl CH_3, J = 0.8 Hz), 1.665 (m, 3 H, vinyl CH_3), 1.8–2.1 (m, 4 H, allylic CH_2), 1.901 (s, 3 H, $COCH_3$), 2.247 (t, 2 H, CH_2COCO, J = 7.3 Hz), 3.929 (t, 2 H, CH_2O, J = 7.3 Hz), 4.61–4.98 (m, 4 H, C=CH_2), 5.106 (br t, 1 H, C-4 vinyl H), 5.58–5.79 (m, 1 H, C-9 vinyl H). This spectrum corresponds closely to the reported[8b] 300-MHz spectrum of natural (–)-**12**. ^{13}C NMR ($CDCl_3$) δ 18.5 (isopropenyl CH_3), 21.0 (acetate CH_3), 23.6 (3-CH_3), 31.3, 31.6, 32.0, 32.0 (C-5,6,7,8), 47.1 (C-2), 62.7 (C-1), 111.6 (isopropenyl CH_2=C), 114.2 (C-9), 126.4 (C-4), 131.1 (C-3), 138.9 (C-10), 147.1 (isopropenyl CH_2=C), 171.0 (C=O).

Upon GLC analysis (6 ft × 0.25 in. column, 10% UCW-98), racemic **14** was found to have the same retention time as the more mobile of the two isomers present in the authentic mixture of isomers. Approximately 2% of the *E* isomer was found to be present in our sample.

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Registry No. 2a, 83199-83-1; (*E*)-**2b**, 83199-84-2; (*E*)-**2c**, 83207-71-0; **6a**, 83199-86-4; **6b**, 83199-87-5; **6c**, 83199-88-6; **6d**, 83199-89-7; **6e**, 83199-90-0; **6f**, 83199-91-1; **6g**, 83199-92-2; **6h**, 83199-93-3; **7**, 35000-38-5; **8b**, 83199-85-3; **11**, 83199-82-0; **13a**, 6137-08-2; **13b**, 49827-45-4; **13c**, 83199-94-4; **13d**, 2550-26-7; **13e**, 83199-95-5; **13f**, 83199-96-6; **13g**, 83199-97-7; **13h**, 83199-98-8; **13** (R_1 = R_2 = R_4 = H; R_3 = Pr), 110-43-0; (±)-(*Z*)-**14**, 66348-55-8; (*Z*)-**18**, 39149-98-9; (*Z*)-**19**, 83199-99-9; (*Z*)-**21**, 83200-00-4; (*Z*)-**22**, 83200-01-5; **23** (R = THP), 83200-02-6; (±)-(*Z*)-**24a**, 83200-03-7; (±)-(*Z*)-**24b**, 83200-04-8; (±)-(*Z*)-**25a**, 83200-05-9; (±)-(*Z*)-**25b**, 83200-06-0; (2-*tert*-butoxy-2-oxoethyl)triphenylphosphonium chloride, 35000-37-4; triphenylphosphine, 603-35-0; *tert*-butyl chloroacetate, 107-59-5; 3-chloropropanoyl chloride, 625-36-5; (*E*)-crotonyl chloride, 625-35-4; (*E*)-cinnamoyl chloride, 17082-09-6; hexanoyl chloride, 142-61-0; 2-lithio-1,3-dithiane, 36049-90-8; hydrocinnamoyl chloride, 645-45-4; methylenetriphenylphosphorane, 3487-44-3; geranyl chloride, 5389-87-7; geranyl bromide, 6138-90-5; (*Z*)-1-chloro-3,7-dimethyl-2,6-octadiene, 20536-36-1; (*Z*)-1-bromo-3,7-dimethyl-2,6-octadiene, 25996-10-5.

Versatile Route to Substituted Ketones through Charge-Directed Conjugate Addition Reactions

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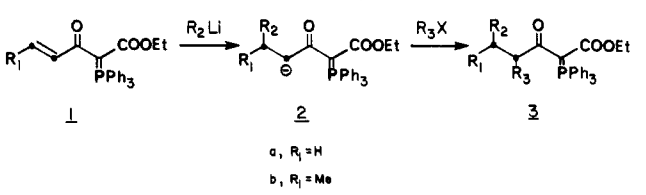
Charge-directed conjugate addition reactions have been applied to the preparation of highly substituted ketones. Acylphosphoranes resulting from conjugate addition–alkylation reactions are reduced by Al–Hg to β-keto esters, which, upon alkylation and hydrolysis, give ketones in high yields. An application of this methodology to the synthesis of **9**, the defense substance of *L. longipes*, is described.

We have previously described the highly efficient charge-directed conjugate addition reactions of a variety of nucleophiles to unsaturated acyl derivatives of (carboethoxymethylene)triphenylphosphorane **1**.[1] These additions give anionic adducts, **2**, that are readily alkylated by ordinary alkyl halides (Scheme I). The elaborated acyl ylide **3** may then be converted to an ester by heating with an alcohol in the presence of an acid.[1a] In the preceding paper[2] we demonstrated the utility of the *tert*-butyl esters

Scheme I



of such ylides in the preparation of methyl ketones through a sequence of manipulations involving decarbalkoxylation of these esters and subsequent hydrolyses of (acylmethylene)triphenylphosphoranes. Ylide manipulations which would lead to more highly substituted ketones would

(1) (a) Cooke, M. P., Jr.; Goswami, R. *J. Am. Chem. Soc.* **1977**, *99*, 642. (b) Cooke, M. P., Jr. *Tetrahedron Lett.* **1979**, 2199.
(2) Cooke, M. P., Jr.; Burman, D. L. *J. Org. Chem.*, preceeding paper in this issue.

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