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Lithium–Halogen Exchange-Initiated Cyclization Reactions. 3. Intramolecular Conjugate Addition Reactions of Unsaturated Acylphosphoranes[1]

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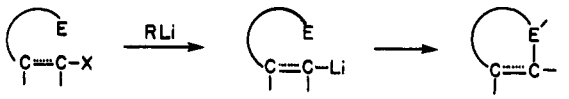
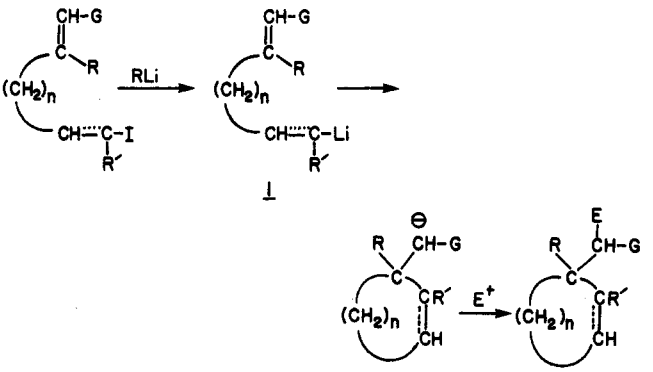
The lithium–halogen exchange-initiated intramolecular conjugate addition reactions of some model unsaturated acylphosphoranes have been examined. The effects of halide type, chain length, and acceptor substitution pattern on the feasibility of ring construction were studied. The lithium–bromine exchange reactions in two 2-bromoaryl acceptors were found to be too slow, relative to competing side reactions, to allow practical carbocycle syntheses while 3-, 4-, 5-, and 6-membered carbocycles are formed in good to excellent yields from precursors that are vinyl and saturated primary iodides. Highly efficient intramolecular conjugate addition reactions to β,β-disubstituted acceptor units are possible, and intermediate anions from intramolecular conjugate addition reactions are readily captured with electrophiles.

Lithium–halogen exchange reactions provide an important method for the introduction of nucleophilic centers.[3] While the mechanistic aspects of these reactions are not entirely clear,[4] many exchange reactions appear to be quite rapid, even at low temperatures. We are currently studying cyclization reactions of the type shown in Scheme I where nucleophilic centers introduced through lithium–halogen exchange reactions subsequently undergo intramolecular bond-forming reactions with an internal electrophilic center. The successful execution of such schemes requires that both the exchange reaction and the cyclization reaction be faster than any irreversible reaction between the metalating reagent and the electrophilic center. Largely through the pioneering work of Parham and co-workers, lithium–halogen exchange reactions in aromatic systems have been shown to be possible in the presence of a variety of common electrophilic groups (COO^-, COOR, CN, $CONR_2$, CX, C=NR, NO_2).[5] On the basis of these studies, a number of exchange-initiated cyclization reactions have been described including cyclialkylation reactions of halides,[5,6] epoxides,[7] ketones,[1] and

Scheme I



Scheme II



(1) Part 2: Cooke, M. P., Jr.; Houpis, I. N. *Tetrahedron Lett.* **1985**, *26*, 4987.

(2) Present address: College of Southern Idaho, Twin Falls, ID 83301.

(3) Wakefield, B. J. *The Chemistry of Organolithium Compounds*; Pergamon: New York, 1974; p 133.

(4) (a) Gilman, H.; Jones, R. G. *Org. React.* **1951**, *6*, 339. (b) Jones, R. G.; Gilman, H. *Chem. Rev.* **1954**, *54*, 835. (c) Schollkopf, U. In *Methoden der Organischen Chemie*; Georg Thieme: Stuttgart, 1970, Vol 13/1. (d) Bailey, W. F.; Gagnier, R. P.; Patricia, J. J. *J. Org. Chem.* **1984**, *49*, 2098. (e) Wittig, G.; Schollkopf, U. *Tetrahedron* **1958**, *3*, 91. (f) Reich, H. J.; Phillips, N. H.; Reich, I. L. *J. Am. Chem. Soc.* **1985**, *107*, 4101. (g) Newcomb, M.; Williams, . G.; Crumpacker, E. L. *Tetrahedron Lett.* **1985**, *26*, 1183. (h) Ashby, E. C.; Pham, T. N.; Park, B. *Tetrahedron Lett.* **1985**, *26*, 4691. (i) Bailey, W. F.; Patricia, J. J.; Nurmi, T. T.; Wang, W. *Ibid.* **1986**, *27*, 1861.

(5) Parham, W. E.; Bradsher, C. K. *Acc. Chem. Res.* **1982**, *15*, 300.

(6) (a) Baker, W.; Buggle, K. M.; McOmie, J. F. W.; Watkins, D. A. M. *J. Chem. Soc.* **1958**, 3594. (b) Brewer, P. D.; Tagat, J.; Hergrueter, C. H.; Helquist, P. *Tetrahedron Lett.* **1977**, 4573. (c) Bailey, W. F.; Gagnier, R. P. *Ibid.* **1982**, *23*, 5123. (d) Boardman, L. P.; Bagheri, V.; Sawada, H.; Negishi, E. *J. Am. Chem. Soc.* **1984**, *106*, 6105. (e) Stoll, H. T.; Negishi, E. *Tetrahedron Lett.* **1985**, *26*, 5671.

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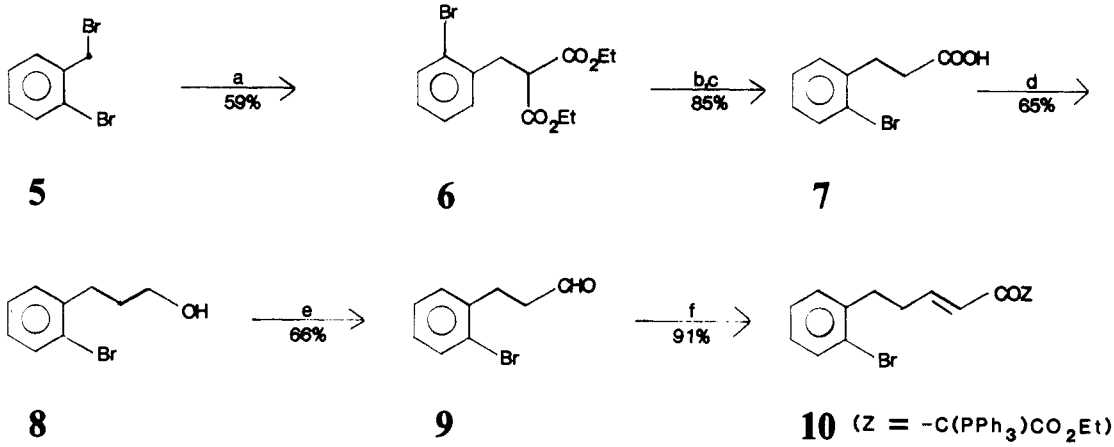
Scheme III[a]



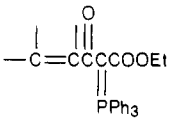
[a] Key: (a) $NaCH(COOEt)_2$; (b) KOH, 90 °C; (c) HCl, H_2O, reflux; (d) BH_3; (e) PCC; (f) 15, NaH.

aldehydes[1] and cycliacylation reactions of carboxylates,[8] amides,[1,9] esters,[1,10] and nitriles.[11]

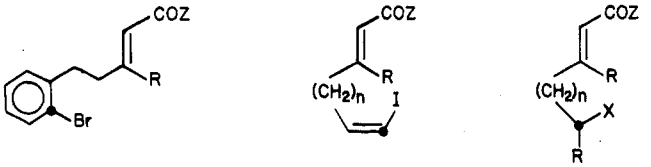
Metal–halogen exchange-initiated cyclization reactions involving additions to carbon–carbon double bonds have only recently begun to receive attention. While the relatively slow intramolecular cyclizations of unactivated olefins have been studied,[12] the only examples involving additions to polarized olefins (Michael or conjugate additions) appear to be our brief study of exchange-initiated cyclization reactions of unsaturated *tert*-butyl esters leading to cyclopentane derivatives[13] and cyclizations involving unsaturated sulfones.[14] We now report the results of a study of lithium–halogen exchange-initiated intramolecular conjugate addition reactions (Scheme II) that examines the effects of chain length, acceptor substitution pattern, and halide type on the feasibility of such reactions.

The execution of Scheme II requires that the lithium–halogen exchange rate be greater than competing reactions involving the metalating agent (RLi) such as reactions with the acceptor unit's polarizing moiety G, direct conjugate addition to the β-carbon of the acceptor moiety and proton abstractions involving acidic (allylic) protons. Additionally, the rate of cyclization of the lithiated exchange-generated cyclization precursor, **1**, must also be greater than nonproductive reactions such as proton abstractions (intramolecular or intermolecular), other intermolecular reactions, and the aforementioned side reactions involving the metalating agent RLi.

For this study we chose to avoid problems arising from reactions of nucleophiles with the polarizing unit, G, by using a Michael acceptor based on an unsaturated acylphosphorane. We have shown this class of Michael acceptor to be highly resistant to nucleophilic attack owing to the charge protection imparted by the neighboring ylide moiety, thereby directing nucleophiles to the β-carbon of the ethylenic unit in what we have termed charge-directed conjugate addition reactions.[15] Furthermore, the acceptors based on these acyl ylides are quite stable,[15] are easily prepared,[15,16] and give anionic Michael adducts that are readily alkylated[15] and subsequently may be converted into esters,[15] acids,[17] ketones,[18] and Wittig-active acylphosphoranes.[18]



We began our study by examining the exchange-initiated cyclization reactions of substrates **2** that contain 2-bromoaryl units insomuch as a report by Whitlock[8b] concluded that (2-bromophenyl)alkanoic acids undergo extraordinarily rapid lithium–bromine exchange reactions.[19] Results from our initial study and from our study of unsaturated *tert*-butyl esters[13] led us to also examine vinyl iodides **3** and saturated halides **4**.



2 3 4

Z= -C(PPh3)COOEt

Synthesis of Cyclization Precursors

Aryl Bromides. Aryl bromide **10** was prepared as shown in Scheme III by the condensation of aldehyde **9** with phosphonate Wittig reagent **15**,[16] the *E* isomer being

(7) (a) Corbel, D.; Durst, T. *J. Org. Chem.* **1976**, *41*, 3648. (b) Bradsher, C. K.; Reames, D. C. *Ibid.* **1978**, *43*, 3800. (c) Corbel, D.; Descesare, J. M.; Durst, T. *Can. J. Chem.* **1978**, *56*, 505. (d) Dhawan, K. L.; Gowland, B. D.; Durst, T. *J. Org. Chem.* **1980**, *45*, 922. (e) Last, L. A.; Fretz, E. R.; Coates, R. M. *Ibid.* **1982**, *47*, 3211. (f) Babler, J. H.; Bauta, W. E. *Tetrahedron Lett.* **1984**, *25*, 4323. (g) Cooke, M. P., Jr.; Houpis, I. N. *Ibid.* **1985**, *26*, 3643.

(8) (a) Parham, W. E.; Jones, L. D.; Sayed, Y. A *J. Org. Chem.* **1975**, *40*, 2394. (b) Boatman, R. J.; Whitlock, B. J.; Whitlock, H. W., Jr. *J. Am. Chem. Soc.* **1977**, *99*, 4822. (c) Negishi, E.; Miller, J. A. *Ibid.* **1983**, *105*, 6761.

(9) Sawada, H.; Webb, M.; Stoll, A. T.; Negishi, E. *Tetrahedron Lett.* **1986**, *27*, 775.

(10) van der Does, T.; Klumpp, G. W.; Schakel, M. *Tetrahedron Lett.* **1986**, *27*, 519.

(11) Larcheveque, M.; Debal, A.; Cuigny, T. *J. Organomet. Chem.* **1975**, *87*, 25.

(12) (a) Bailey, W. F.; Patricia, J. J.; Del Gobbo, V. C.; Jarret, R. M.; Okarma, P. J. *J. Org. Chem.* **1985**, *50*, 1999. (b) Chamberlin, A. R.; Bloom, S. H. *Tetrahedron Lett.* **1986**, *27*, 551.

(13) Cooke, M. P., Jr. *J. Org. Chem.* **1984**, *49*, 1144.

(14) Hamann, P. R.; Toth, J. E.; Fuchs, P. L. *Ibid.* **1984**, *49*, 3865.

(15) Cooke, M. P., Jr.; Goswami, R. *J. Am. Chem. Soc.* **1977**, *99*, 642.

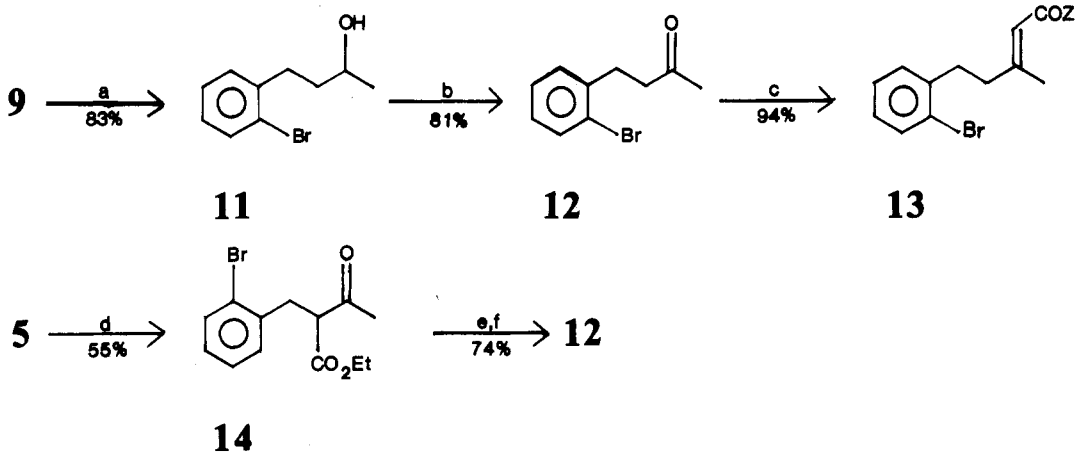
(16) Cooke, M. P., Jr.; Biciunas, K. P. *Synthesis* **1981**, 283.

(17) Cooke, M. P., Jr. *J. Org. Chem.* **1983**, *48*, 744.

(18) Cooke, M. P., Jr.; Burman, D. L. *J. Org. Chem.* **1982**, *47*, 4955. Cooke, M. P., Jr. *Ibid.* **1982**, *47*, 4963.

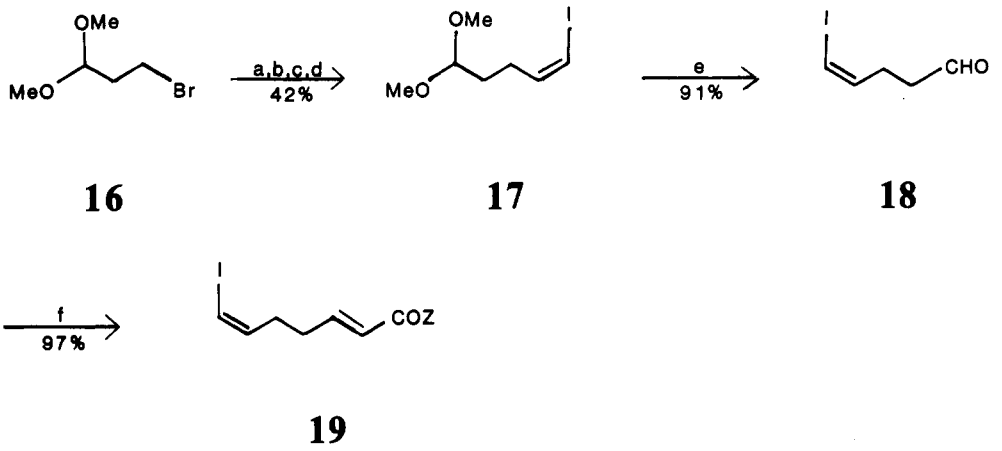
(19) This conclusion has recently been challenged: Beak, P.; Chen, C.-W. *Tetrahedron Lett.* **1985**, *26*, 4979.

Scheme IV[a]



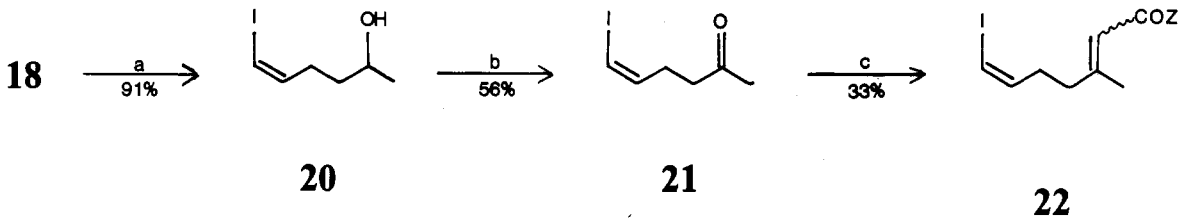
[a] Key: (a) MeLi; (b) PCC; (c) 15, NaH; (d) $CH_3COCHNaCOOEt$; (e) NaOH, H_2O, reflux; (f) HCl.

Scheme V[a]



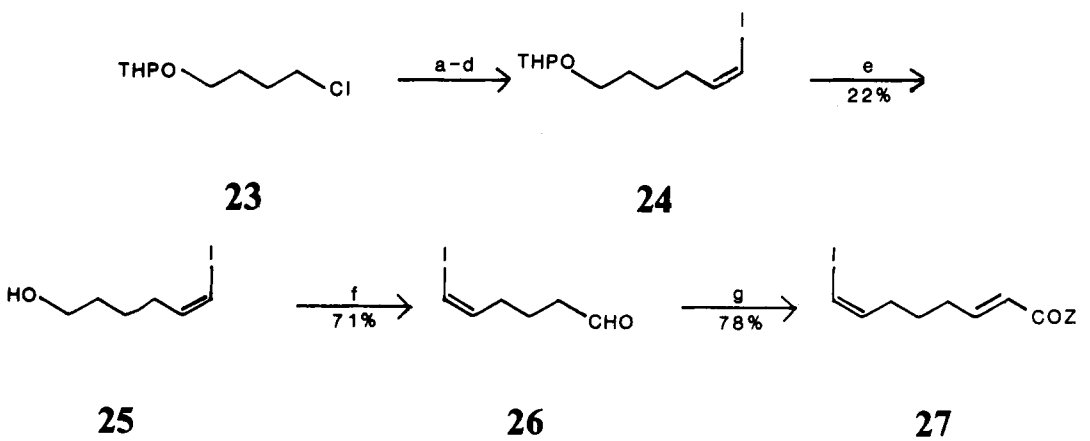
[a] Key: (a) Mg; (b) CuBr·Me_2S; (c) HC≡CH; (d) I_2; (e) 50% HOAc; (f) 15, NaH.

Scheme VI[a]

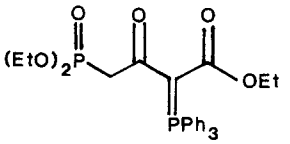


[a] Key: (a) MeMgBr; (b) PCC; (c) 15, NaH.

Scheme VII[a]



[a] Key: (a) Mg; (b) CuBr·Me_2S; (c) HC≡CH; (d) I_2; (e) 60% HOAc; (f) PCC; (g) 15, NaH.



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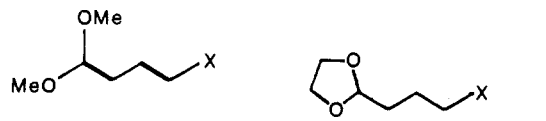
obtained in high yield. Aldehyde **9** was prepared from *o*-bromobenzyl bromide (**5**) in a straightforward manner by a malonic ester synthesis to carboxylic acid **7**, reduction with BH_3 to the corresponding alcohol **8**, and oxidation with pyridinium chlorochromate (PCC). This aldehyde was also used in the preparation of β,β-disubstituted acceptor **13** as shown in Scheme IV. Treatment of **9** with MeLi followed by PCC oxidation gave ketone **12** which, upon Horner–Wittig condensation with **15**, gave acceptor **13** as a 7:3 mixture of *E* and *Z* isomers. The pure *E* isomer, used in subsequent cyclization studies, could be obtained by chromatography and recrystallization. Ketone **12** was also prepared by an acetoacetic ester synthesis proceeding through keto ester **14**.

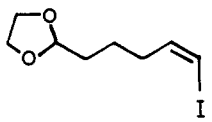
Vinyl Iodides. Construction of the *cis*-vinyl iodide unit needed for substrates **3** was achieved in each case by the copper-catalyzed Normant addition of functionalized Grignard reagents to acetylene and iodination of the resulting vinylcopper intermediate.[20] In this manner intermediate **17** was obtained as shown in Scheme V. Hydrolysis of **17** gave aldehyde **18** which, upon Horner–Wittig condensation with **15**, gave cyclization precursor **19**. The β-methyl analogue **22** was prepared by the addition of MeMgBr to **18** and oxidation of this alcohol to ketone **21** (Scheme VI). Condensation of this ketone with phosphonate **15** gave **22** as a 3:1 mixture of 4-*E* and 4-*Z* isomers that were not separated.

The preparation of 6-membered ring precursor **27**, in a manner analogous to the route used to prepared **19** (Scheme V), was somewhat more problematical. We were



28 a (X = Cl) b (X = I)

29 a (X = Cl) b (X = I)



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unable to prepare the prerequisite Grignard reagents from either **28a** or **28b** in either THF or Et_2O. Attempts to prepare the previously reported[21] Grignard reagent from **29a** in THF were more successful, but application of the Normant addition–iodination procedure generally gave, in low yields, mixtures of **30** and **29b**—the latter product presumably resulting from halogen exchange in unreacted chloride **29a**. While small amounts of pure **30** could be obtained from these mixtures by the selective destruction of **29b** (1:1 Et_3N–EtOH, 80 °C, 8 h), we abandoned this route in favor of the one shown in Scheme VII.

Normant addition of the Grignard reagent prepared from **23** to acetylene followed by iodination gave the desired vinyl iodide **24** along with varying amounts of the free alcohol **25**. By direct hydrolysis of the crude product (60% HOAc), pure **25** could be obtained in 22% overall yield. Oxidation of **25** with PCC and olefination with **15** gave the desired cyclization precursor **27** in good yield.

Saturated Halides. Cyclization substrates **4** could, in general, be prepared in good yields by the olefination of the corresponding halocarbonyl compounds with ylide phosphonate **15**, except in cases where the halocarbonyl component was base sensitive. Surprisingly, we were able to convert aldehyde **31** directly into the corresponding unsaturated ylide **32** as shown in Scheme VIII. Hydroxyl group exposure followed by halide ion displacements from methanesulfonate ester **34** gave **36**.

Unsaturated ylide **43** could not be prepared by the condensation of 4-chlorobutanal (**37**) with either the sodium or lithium salts of phosphonate **15**, presumably owing to the ease with which γ-halocarbonyl compounds undergo base-promoted conversions to cyclopropyl derivatives.[22] Fortunately, the desired olefination was successful using the apparently less basic sodium salt of triethyl phosphonoacetate (Scheme IX). The resulting ethyl ester **39** was converted via its acid chloride to chloro ylide **43**, which gave the required cyclization precursor **45** upon halide exchange. The homologous ylide **46** had also been prepared[23] by this scheme prior to our development of phosphonate **15**, and we have no reason to believe that it could not be prepared directly from **15** and 5-chloropentanal (**38**). 6-Chlorohexanal (**48**) was uneventfully converted to unsaturated ylide **49** with **15** and subsequently to cyclization precursor **50** by halide exchange (Scheme X).

The preparation of β,β-disubstituted cyclization precursors **55** and **58** are shown in Schemes XI and XII, respectively. In the case of **55**, the sensitivity of γ-chloro ketone **51** to base again precluded its direct conversion to **54** with phosphonate reagent **15**. Fortunately, **52** could be obtained as a mixture of isomers by the condensation of **51** with the sodium salt of triethyl phosphonoacetate and subsequently converted into **55** as previously discussed in Scheme IX. The *E* isomer of **55** could be obtained by chromatography and was used for cyclization studies. Ylide **57** (Scheme XII) was obtained by the direct condensation of δ-chloro ketone **56** with **15** as a 3:1 mixture of *E* and *Z* isomers. The isomers were separated by chromatography after halide exchange, and *E*-**58** was used in cyclization studies.

Secondary iodide **60** was prepared as shown in Scheme XIII from known 4-bromopentanal.[24] Despite the fact that the precursor is a γ-halo aldehyde, **59** could be obtained, albeit in low yield, by a direct condensation with phosphonate **15**. Halide exchange using NaI then gave **60**.

Cyclization Studies

Aryl Bromides. Treatment of bromide **10** with 1.0 equiv of *n*-BuLi in THF at −78 °C gave, after protic quenching, **61** in 77% yield. When 2 equiv of *n*-BuLi was

(20) (a) Normant, J. F.; Alexakis, A. *Synthesis* **1981**, 841. (b) Westmijze, H.; Meijer, J.; Vermeer, P. *Recl. Trav. Chim. (Pays-Bas)* **1977**, *96*, 168. (c) Westmijze, H.; Meizer, J.; Box, H. J. T.; Vermeer, P. *Ibid.* **1976**, *95*, 299.

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(22) Bartsch, R. A.; Cook, D. M. *J. Org. Chem.* **1970**, *35*, 1714.

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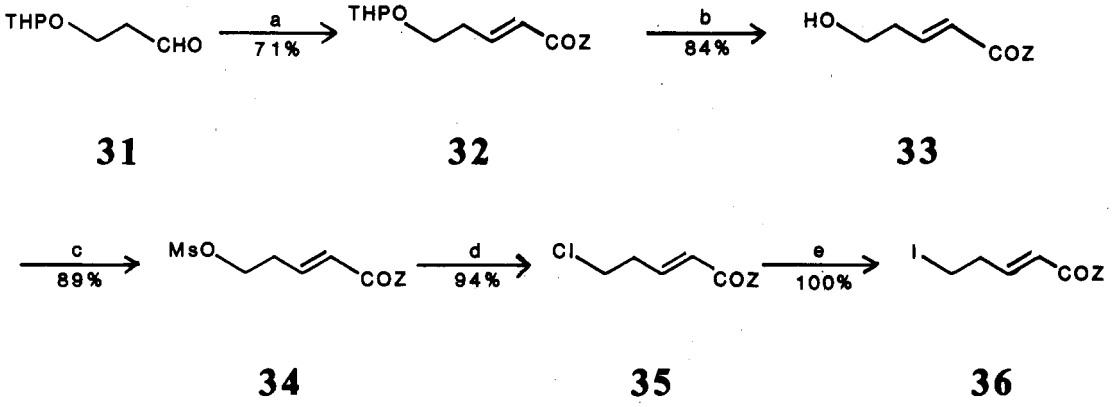
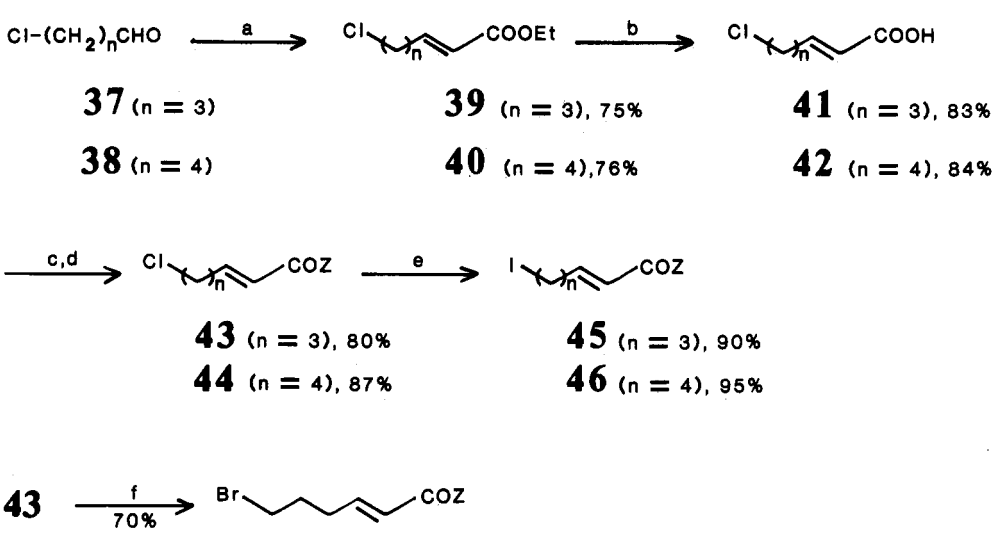
(24) Obol'nikova, E. A.; Samokhvalov, G. I. *J. Gen. Chem. USSR* **1962**, *32*, 3489.

Scheme VIII[a]



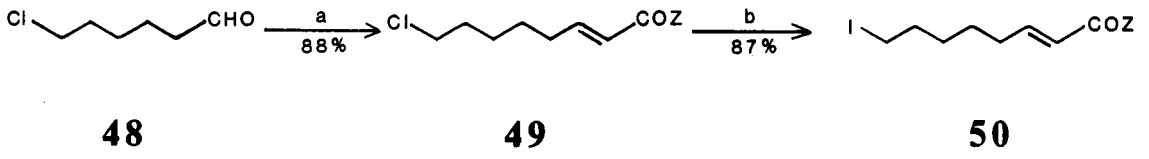
[a] Key: (a) 15, *n*-BuLi; (b) py·HOTs, EtOH; (c) MsCl, pyridine; (d) LiCl, DMF; (e) NaI.

Scheme IX[a]



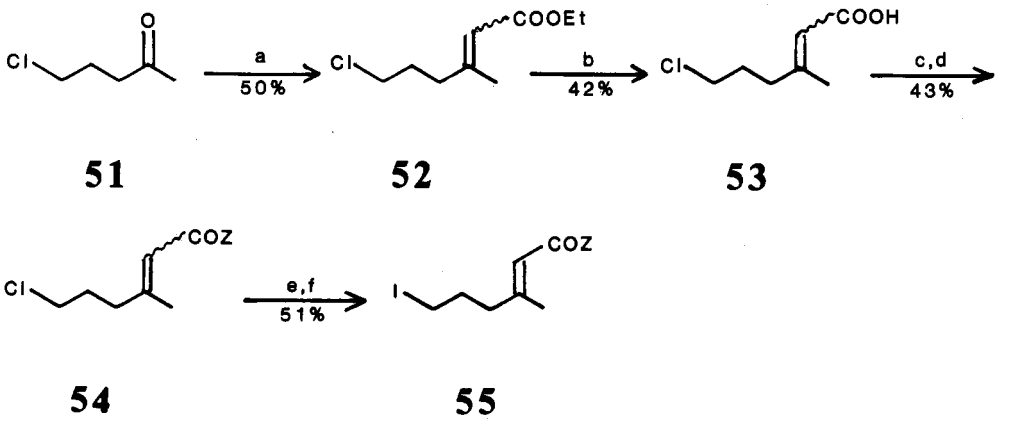
[a] Key: (a) $(EtO)_2P(O)CH_2COOEt$, NaH; (b) KOH; H^+; (c) $(COCl)_2$; (d) $Ph_3P{=}CHCOOEt$; (e) NaI; (f) NaBr, NMP.

Scheme X[a]

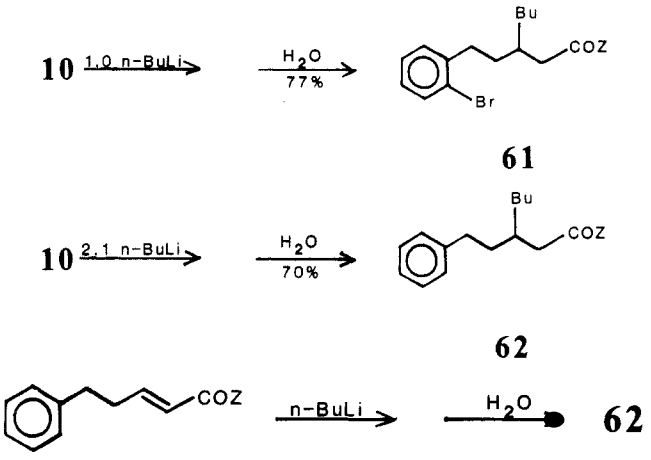


[a] Key: (a) 15, NaH; (b) NaI.

Scheme XI[a]



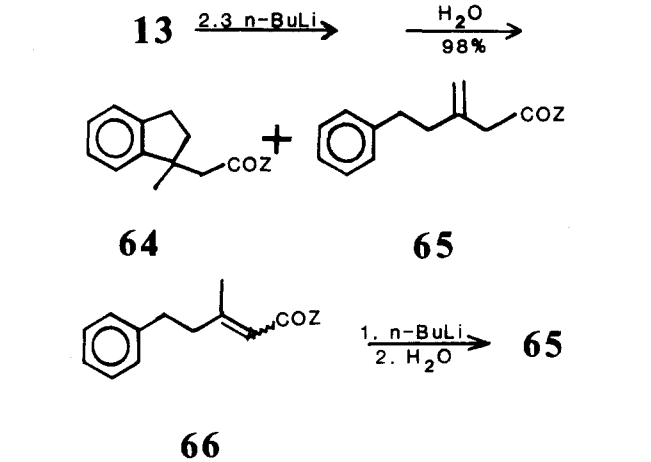
[a] Key: (a) $(EtO)_2P(O)CH_2COOEt$, NaH; (b) KOH, H^+; (c) $(COCl)_2$; (d) $Ph_3P{=}CHCOOEt$; (e) NaI; (f) PTLC.



employed, **62** was obtained in 70% yield. This product was identical with the one obtained from the addition of *n*-BuLi to **63**. In no case was any cyclization product observed. Clearly, in this substrate, the rate of direct conjugate addition of *n*-BuLi to the unsaturated ylide unit is faster than the desired metal–halogen exchange reaction. With excess metalating agent, exchange does occur, after addition, giving rise to debrominated adduct **62** upon protonation of the intermediate lithiated enolate.

We also attempted to induce cyclization by direct reaction of **10** with magnesium and lithium—having been successful previously with the Grignard-initiated cyclization of **46** and **50**.[23] All attempts failed, however. Treatment of **10** in THF with magnesium (activated with ethylene dibromide) gave only unidentified non-halogen-containing products of low chromatographic mobility, and efforts with lithium were likewise unsuccessful.

We anticipated that more success would be encountered in exchange-initiated cyclizations of **13**, since we had previously shown that intermolecular conjugate additions do not normally occur with β,β-disubstituted ylides of this type.[15] Indeed, treatment of **13** with excess *n*-BuLi gave,



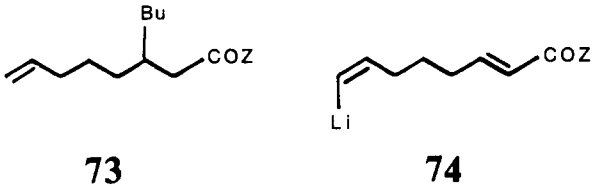
after protic quenching, an inseparable mixture that contained the desired cyclization product **64** along with olefin **65** (**64**:**65** = 2.5). Similar results were obtained at −100 °C and when using only 1 equiv of *n*-BuLi. Thus, while the rates of lithium–halogen exchange and subsequent cyclization exceed the rate of direct addition of *n*-BuLi to the activated olefin, allylic proton abstraction from the β-methyl group is competitive, giving rise to **65** through kinetic quenching of the intermediate dienolate anion. Ylide **65** was also obtained by quenching the dienolate anion obtained from **66** (a 4:1 mixture of *E* to *Z* isomers from the condensation of 4-phenyl-2-propanone with **15**) with water.

While partial success was achieved in cyclizing **13**, these studies have demonstrated that the rate of metal–halogen exchange in ortho-brominated aryl systems of this type is not sufficiently rapid to enable practical ring construction by this technique. Studies with vinyl iodides (vide infra) suggest that cyclizations might be successful with iodinated analogues, but we have not yet explored such models.

Vinyl Iodides. Exchange-initiated cyclization reactions of vinyl iodides leading to 5- and 6-membered ring carbocycles proved highly successful (Table I). Treatment of **19** with *n*-BuLi gave, after protic quenching of the intermediate anion, **66** in 87% yield (entry 1). Six-membered ring formation was equally successful (entry 5). Intermediate enolate anions could be efficiently captured with other electrophiles when *t*-BuLi (2 equiv) was employed as the initiating reagent (entries 2, 3, and 6). The use of *t*-BuLi avoids interference in the alkylation step by the iodide produced in the lithium–iodine exchange reaction (*n*-BuI with *n*-BuLi) insomuch as the second equivalent of *t*-BuLi apparently annihilates exchange-generated *t*-BuI.[25] In each case, alkylation products were a mixture of two diastereomers. Alkylation reactions of ylide anions of this type have previously been found to be exceptionally clean,[15] and only in the alkylation of the intermediate generated from **19** (entry 3) with methyl bromoacetate was a significant side reaction observed. In this case, an unstable product, containing a low-field multiplet at 5.3 ppm in its ^{1}H NMR spectrum and which could be reduced with Ph_3P to **66**, was isolated in 32% yield and is believed to be α-bromo ylide **69** resulting from enolate bromination.

The successful cyclization of **22** is especially noteworthy in that this closure involves the conjugate addition to a β,β-disubstituted olefinic center—a reaction process that we previously have been unable to execute with intermolecular addition reactions.[15]

We also have obtained evidence that the cyclization reaction leading to 6-membered ring-containing **71** (entry 5) proceeds at a slower rate than in the corresponding formation of cyclopentane derivative **66**. When cyclization reactions of **27** were conducted by the addition of excess *n*-BuLi at −78 °C in under 2 min, appreciable amounts of **73** were observed in up to 20% yield in addition to **71**

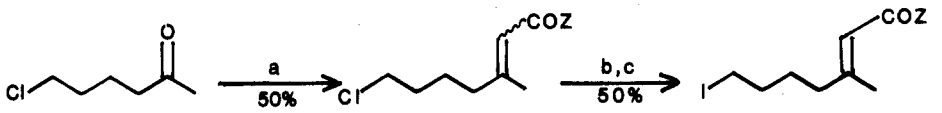


(43%). Longer addition times (>4 min) reduced the production of **73** to only 4%. This suggests that the rate of ring closure of lithium intermediate **74** is slow enough to allow for some intermolecular conjugate addition of excess *n*-BuLi to **74** to occur, thereby producing a dilithiated intermediate that gives **73** upon protic workup. No such interceptions of the vinyllithium intermediates leading to 5-membered ring-containing **66** or **70** were observed under similar conditions.

Saturated Iodides. Saturated iodides of type **4** (X = I, R = H) successfully underwent exchange-initiated ring-closure reactions in every case (Table II), and 3-, 4-, and 5-membered carbocycles (entries 1–4, 6, and 7) were

(25) (a) Corey, E. S.; Beames, D. J. *J. Am. Chem. Soc.* **1972**, *94*, 7210. (b) Seebach, D.; Neumann, H. *Chem. Ber.* **1974**, *107*, 847.

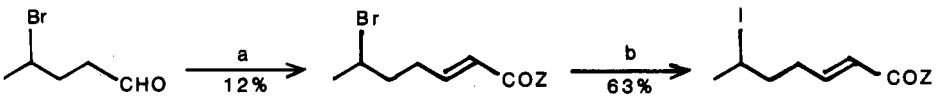
Scheme XII[a]



56 **57** **58**

[a] Key: (a) **15**, NaH; (b) PTLC; (c) NaI.

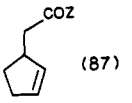
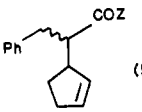
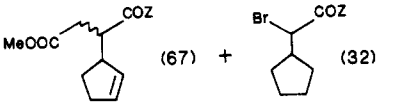
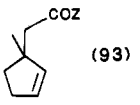
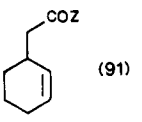
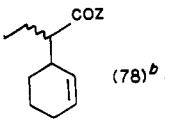
Scheme XIII[a]



59 **60**

[a] Key: (a) **15**, NaH; (b) NaI.

Table I. Cyclization of Vinyl Iodides (Scheme II)[a]

entry	iodide	RLi	electrophile	product (yield, %)
1	**19**	*n*-BuLi	H_2O	 (87) **66**
2		*t*-BuLi	$PhCH_2Br$	 (91) **67**
3		*t*-BuLi	$BrCH_2COOMe$	 (67) + (32) **68** **69**
4	**22**	*n*-BuLi	MeOH	 (93) **70**
5	**27**	*n*-BuLi	MeOH	 (91) **71**
6		*t*-BuLi	EtI	 (78)[b] **72**

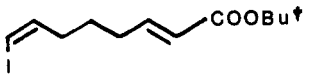
[a] RLi added to iodide in THF at −78 °C. [b] Unalkylated **71** present in 11% yield.

produced in uniformly good yields. It should be noted that while the exchange reactions of these primary saturated iodides with *n*-BuLi would be expected to have equilibrium constants near unity,[26] the rates of these reactions, as well as those of most of the subsequent ring closures, are apparently so rapid relative to the conjugate addition of *n*-BuLi to the acceptor as to make the equilibrium constant unimportant. Iodide **50** gave cyclohexyl derivative **79** in only 44% yield, however. The lower yield in this case is likely the result of a slower rate of ring closure as was observed with the corresponding vinyl iodide **27** which, with the more reactive saturated lithium intermediate, gives rise to increased production of side products at the expense of the desired cyclization product. Surprisingly, products that one might anticipate arising through intramolecular allylic proton abstraction were not observed. In the case of unsaturated analogue **27**, exchange with *n*-BuLi rapidly produces a more stable vinyllithium intermediate, essentially irreversibly,[26] perhaps providing increased

(26) Applequist, D. E.; O'Brien, D. F. *J. Am. Chem. Soc.* **1963**, *85*, 743.

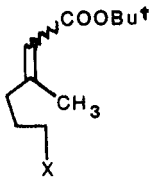
tolerance to the slower rate of ring closure. It is interesting to note that the corresponding 6-membered ring-forming exchange-initiated cyclization reaction of unsaturated ester **85** likewise proceeds in poor yield (14%) under similar conditions,[13] while the corresponding vinyl iodide **86** undergoes cyclization in 59% yield.[27]

85



86

As in the case of the cyclizations of vinyl iodides, cyclizations involving intramolecular additions to β,β-disubstituted acceptor units (entries 6 and 7) were successful. It is noteworthy that in the attempted cyclization of unsaturated ester **87a** allylic proton abstraction preempted



87 a (X = I)
b (X = Li)

intramolecular conjugate addition.[13] This is presumably the result of a more favorable transition state in which the nucleophilic center in the lithiated intermediate **87b** can approach a proton of the β-methyl group more nearly along its C–H axis.[28] While this same favorable situation for proton abstraction would appear to be present in the lithiated intermediates derived from **55** and **58**, it is possible that a lower kinetic acidity of the allylic protons in these unsaturated acyl ylides may be responsible for the preeminence of the conjugate addition pathway. It is also possible that the cyclizations involving the unsaturated ylides and esters proceed via different pathways[29] or that ylide additions proceed at a faster rate.

We have examined one case involving a primary saturated bromide. Treatment of **47** with *n*-BuLi gave carbocycle **82** in 87% yield (entry 8). In this case the direct addition of *n*-BuLi to the acceptor unit is faster than bromine–lithium exchange and the carbocycle resulting from an intramolecular alkylation of the addition-generated enolate is produced. This type of reaction was previously observed with the corresponding chloride.[23]

Finally, we investigated the feasibility of initiating cyclizations with precursors that are secondary iodides. Treatment of **61** with *n*-BuLi (entry 9) gave a complex mixture from which two products containing extremely similar ^{1}H NMR spectra were obtained in a combined yield of 48%. On the basis of spectral evidence (see the Experimental Section), these are believed to be stereoisomers of **83**, resulting from the direct addition of *n*-BuLi to the acceptor unit followed by an intramolecular alkylation of the resulting enolate. Small amounts (8%) of a mixture of products containing olefinic peaks at 5.0 and 5.35 ppm and a doublet at 2.82 ppm (characteristic of α-methylene units in acyclic addition adducts) were also obtained. While not well characterized, these products seem likely to be isomers **84** resulting from *n*-BuLi addition and dehydroiodination rather than alkylation. It thus appears that the rate of lithium–iodine exchange with *n*-BuLi and secondary iodides is too slow to compete with the intermolecular addition of *n*-BuLi to the acceptor unit.

Conclusions

The rates of lithium–halogen exchange reactions in THF between alkyllithium reagents and aryl bromides, alkyl bromides, and secondary iodides are slower than the rates of the intermolecular conjugate addition reactions of unsaturated acyl phosphoranes, while the exchange rates of vinyl and primary alkyl iodides are faster. Thus, exchange-initiated reactions of cyclization precursors containing the latter types of halides may be used to form 3-, 4-, 5-, and 6-membered rings in excellent yields. For the formation of 6-membered carbocycles, it appears to be more efficient to use precursors that are vinyl iodides rather than saturated iodides.

Cyclizations involving intramolecular conjugate additions to fully substituted olefinic centers are quite feasible in contrast to their intermolecular counterparts. Additionally, intramolecular proton abstractions from allylic positions have not been observed to thwart cyclization reactions in unsaturated acyl ylides.

In summary, the extremely rapid lithium–halogen exchange reactions of both vinyl and saturated primary iodides have been shown to make exchange-initiated intramolecular conjugate addition reactions potentially useful for the construction of functionalized carbocycles. We are currently examining the application of such reactions to the construction of polycyclic ring systems.

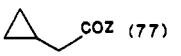
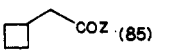
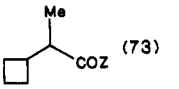
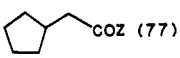
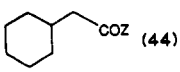
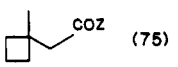
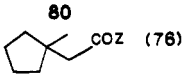
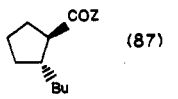
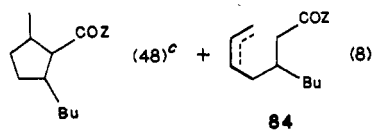
Experimental Section

General Methods. Infrared spectra (IR) were recorded as films (neat) or as solutions ($CHCl_3$, 0.1 mm) with a Beckman AccuLab 1 spectrometer. NMR spectra were recorded at 60 MHz (^{1}H) with a Varian EM-360 spectrometer, at 100 MHz (^{1}H) with a JEOL MH-100 spectrometer, at 90 MHz (^{1}H) and 22.5 MHz (^{13}C) with a JEOL FX-90q spectrometer, at 22.6 MHz (^{13}C) with a Bruker WH-90 spectrometer, and at 200 MHz (^{1}H) with a Nicolet NT-200 spectrometer. Chemical shifts are reported in δ units downfield from Me_4Si. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; and br, broad band. Operations involving solvent removal under reduced pressure refer to use of a Buchi rotoevaporator operated at water aspirator pressure. 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 and boiling points are uncorrected. Analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN.

All reactions involving air-sensitive materials were conducted under an argon atmosphere. For reactions said to be conducted at −78 °C a dry ice–acetone bath was employed while those conducted at −100 °C used a MeOH liquid–solid bath cooled with liquid N_2. Alkyllithium reagents were obtained from Aldrich Chemical Co. and titrated[30] prior to use. Tetrahydrofuran (THF) was distilled from sodium–benzophenone ketyl prior to use.

(27) Unpublished results (M.P.C.).
(28) (a) Grandour, R. D. *Tetrahedron Lett.* **1974**, 295. (b) Menger, F. M.; Chow, J. F.; Kaiserman, H.; Vasquez, P. C. *J. Am. Chem. Soc.* **1983**, *105*, 4996.
(29) The absence of rearrangement products in the intermolecular reactions of 5-hexenyllithium or (cyclopropylmethyl)lithium with unsaturated acyl ylides suggests that the addition step does not proceed by an SET pathway: Biciunas, K., unpublished results.
(30) Watson, S. C.; Eastham, S. F. *J. Organomet. Chem.* **1967**, *9*, 165.

Table II. Cyclization of Saturated Iodides (Scheme II)[a]

entry	iodide	RLi	electrophile	product (yield, %)
1	**36**	*n*-BuLi	H_2O	 (77) **75**
2	**45**	*n*-BuLi	MeOH	 (85) **76**
3		*t*-BuLi	MeI	 (73) **77**
4	**46**	*n*-BuLi[b]	MeOH	 (77) **78**
5	**50**	*n*-BuLi[b]	MeOH	 (44) **79**
6	**55**	*n*-BuLi	EtOH	 (75) **80**
7	**58**	*n*-BuLi[b]	EtOH	 (76) **81**
8	**47**	*n*-BuLi[b]		 (87) **82**
9	**61**	*n*-BuLi	MeOH	 (48)[c] + (8) **83** **84**

[a] RLi added to iodide in THF at −78 °C. [b] RLi addition at −100 °C. [c] Two isomers.

Diethyl (*o*-Bromobenzyl)malonate (6). By a modification of a literature procedure,[31] sodium (14.1 g, 0.61 mol) was dissolved in 300 mL of absolute EtOH, and at 45 °C this solution was treated dropwise with 102.5 g (0.64 mol) of diethyl malonate over 20 min. After 20 min, the solution was cooled to 25 °C and 145.2 g (0.58 mol) of *o*-bromobenzyl bromide[31] was added in one portion. The exothermic reaction was allowed to heat to 70 °C, and when the reaction mixture had cooled to 25 °C, additional EtOH was added (50 mL) and the mixture was then heated in an 85 °C oil bath for 1 h. The ethanol was removed under reduced pressure, and the residue was treated with 200 mL of water and extracted with 100 mL of diethyl ether. Concentration of the dried extract (Na_2SO_4) followed by distillation gave 113 g (59%) of **6**: bp 135–143 °C (0.5 mm) [lit.[32] bp 165–170 °C (3 mm)]; ^{1}H NMR (CCl_4, 60 MHz) δ 1.20 (t, 6 H, OCH_2CH_3, J = 7 Hz), 3.30 (m, 2 H, CH_2), 3.78 (m, 1 H, CH), 4.18 (q, 4 H, OCH_2), 7.0–7.8 (m, 4 H, aromatic).

3-(2-Bromophenyl)propanoic Acid (7). By a modification of a published procedure,[32] a mixture of 93 g (1.4 mol) of 85% KOH, 350 mL of water, and 174 g (0.53 mol) of **6** was stirred at 90–100 °C for 2 h. The EtOH was removed under reduced pressure, and the clear solution was decanted from a small amount of insoluble yellow oil. Cooling of the solution and the addition of 100 mL of concentrated HCl gave the diacid, which was collected by filtration and heated at 130–195 °C for several hours in a 500-mL flask. When CO_2 evolution had ceased, the mixture was allowed to cool to 130 °C and 150 mL of H_2O was slowly added. After the mixture was allowed to stand overnight at room temperature, the pH was adjusted to approximately 2–3 with concentrated hydrochloric acid and the precipitate was collected by filtration and dried, giving 103 g (85%) of **7**: mp 95–97 °C (lit.[33] 99–101 °C); ^{1}H NMR ($CDCl_3$, 100 MHz) δ 2.4–3.4 (m, 4 H, CH_2), 7.0–7.8 (m, 4 H, Ar), 11.0 (br s, 1 H, COOH).

3-(2-Bromophenyl)-1-propanol (8). A solution containing 13.2 g (57.6 mmol) of **7** in 300 mL of THF was stirred at 0 °C under an argon atmosphere while 76 mL (76 mmol) of 1.0 M BH_3–THF were added dropwise during 1 h. The mixture was stirred at 25 °C for 1 h and then heated with 100 mL of 50% aqueous THF. After 2 h, 3.0 g of K_2CO_3 and 200 mL of Et_2O were added and the organic layer was separated, washed with brine, and dried over Na_2SO_4. Solvent removal and distillation gave 8.1 g (65%) of **8**: bp 100–115 °C (0.1 mm) [lit.[34] bp 106–108 (0.5 mm)]; ^{1}H NMR (CCl_4, 60 MHz) δ 1.4–2.2 (m, 2 H, CH_2CH_2O), 2.65–3.10 (m, 2 H, $ArCH_2$), 3.68 (t, 2 H, CH_2O, J = 7 Hz), 4.73 (s, 1 H, OH), 7.0–7.8 (m, 4 H, Ar).

3-(2-Bromophenyl)propanal (9). To a stirred mixture of 7.0 g (32.4 mmol) of pyridinium chlorochromate in 65 mL of CH_2Cl_2 at 25 °C was rapidly added 5.70 g (26.7 mmol) of 3-(2-bromophenyl)propanol (**8**). After 3 h, 300 mL of Et_2O was added, and after stirring for 30 min the organic phase was decanted from the dark residue of chromium salts. The residue was twice extracted with fresh Et_2O (100 mL), and the combined extracts were filtered

(31) Letsinger, R. L.; Skoog, S. H. *J. Am. Chem. Soc.* **1955**, *77*, 5176.
(32) Nakazaki, M.; Yamagami, K.; Isoe, S. *Bull. Chem. Soc. Jpn.* **1961**, 1189.
(33) Parham, W. E.; Jones, L. D.; Sayed, Y. *J. Org. Chem.* **1975**, *40*, 2394.
(34) Berry, M. H.; Frederlick, G. M. *J. Chem. Soc.* **1951**, 412.

through a 10-cm plug of silica gel. Solvent removal and distillation gave 3.70 g (66%) of **9**: bp 95–105 °C (0.1–0.2 mm); IR (neat) ν 3050, 2925, 2820, 2720, 1718, 1564, 1465, 1436, 1014, 743 cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 2.5–3.3 (m, 4 H, CH_2), 7.0–7.8 (m, 4 H, Ar), 9.95 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 22.6 MHz) δ 28.6 (C-3), 43.6 (C-2), 124.2, 127.6, 128.0, 130.4, 132.8, 139.7 (Ph), 200.8 (C-1). Oxime: mp 91.5–92.5 °C. Anal. Calcd for $C_9H_{10}BrNO$: C, 47.34; H, 4.42; N, 6.14. Found: C, 47.57; H, 4.50; N, 6.09.

Ethyl 7-(2-Bromophenyl)-3-oxo-2-(triphenylphosphoranylidine)-4(*E*)-heptenoate (10). To a stirred slurry of 11.0 mmol of NaH in 50 mL of THF was added 3 drops of 2-propanol and 6.05 g (11.5 mmol) of diethyl 2,4-dioxo-4-ethoxy-3-(triphenylphosphoranylidene)butanephosphonate (**15**).[16] After 15 min, a solution of 2.13 g (10.0 mmol) of **9** in 6 mL of THF was added in one portion. Upon completion of the reaction (approximately 40 min as judged by TLC [silica gel, 10:1 CH_2Cl_2–EtOAc)], the solution phase was decanted from the gummy phosphate residue. This residue was further extracted with 100 mL of CH_2Cl_2 and the combined solutions were concentrated, giving an oil, which upon column chromatography (SiO_2, 38 × 5 cm, CH_2Cl_2 then 10:1 CH_2Cl_2–EtOAc), gave 5.35 g (91%) of **10** as an oil that crystallized. An analytical sample was obtained by recrystallization from EtOAc–hexane: mp 89–90 °C; IR ($CHCl_3$) ν 3000, 1657, 1640, 1440, 1370, 1290, 1100, 1090 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 0.66 (t, 3 H, CH_2CH_3, J = 7.5 Hz), 2.52 (m, 2 H, CH_2CH=C), 2.87 (m, 2 H, $ArCH_2$), 3.70 (q, 2 H, OCH_2), 6.9 (m, 1 H, CHCO), 7.2–7.9 (m, 20 H, Ar and CH=CHCO); ^{13}C NMR ($CDCl_3$, 22.6 MHz) δ 13.7 (OCC), 32.6 (C-7), 35.4 (C-6), 58.6 (OC), 71.5 (d, $^1J_{CP}$ = 110.5 Hz), (Ph_3P) 127.1 (d, $^1J_{CP}$ = 94.1 Hz), 128.5 (d, $^2J_{CP}$ = 13.2 Hz), 131.5 (d, $^4J_{CP}$ = 2.9 Hz), 133.1 (d, $^3J_{CP}$ = 10.3 Hz), (Ar) 124.5, 127.5, 128.2, 130.4, 132.9, 141.2, 129.3 (C-4), 139.8 (C-5), 167.7 (d, $^2J_{CP}$ = 14.7 Hz, C-1), 186.6 (d, $^2J_{CP}$ = 4.4 Hz, C-3). Anal. Calcd for $C_{33}H_{30}BrO_3P$: C, 67.70; H, 5.16. Found: C, 67.56; H, 5.09.

4-(2-Bromophenyl)-2-butanone (12). A. To a stirred solution of 10 mmol of CH_3Li in 30 mL of Et_2O at 0 °C was added 2.13 g (10 mmol) of 3-(2-bromophenyl)propanal (**9**) in 25 mL of Et_2O over 30 min. After the mixture was allowed to stand overnight, 12 mL of 1 N HCl was added. The ether layer was separated, washed with brine, and dried over Na_2SO_4. Concentration and distillation gave 1.89 g (83%) of alcohol **11**: bp 110–115 °C (0.1 mm); ^1H NMR (CCl_4, 60 MHz) δ 1.22 (d, 3 H, CH_3, J = 6 Hz), 1.4–2.0 (m, 2 H, CH_2CH), 2.6–3.0 (m, 2 H, CH_2Ar), 3.15 (s, 1 H, OH), 3.85 (m, 1 H, CHO), 6.9–7.7 (m, 4 H, Ar). Without further purification this alcohol (3.48 g, 15.2 mmol) was added with stirring to 3.65 g (16.9 mmol) of pyridinium chlorochromate in 50 mL of CH_2Cl_2. After 3 h, 100 mL of Et_2O was added and the mobile phase was decanted from the black gummy residue that was further extracted with 50 mL of CH_2Cl_2. The combined solutions were filtered through a short plug of silica gel and concentrated. Distillation gave 2.78 g (81%) of **12**: bp 96–101 °C (0.1 mm) [lit.[35] bp 139–140 °C (10 mm)]; ^1H NMR ($CDCl_3$, 100 MHz) δ 2.09 (s, 3 H, CH_3), 2.8–3.1 (m, 4 H, CH_2) 6.9–7.7 (m, 4 H, Ar); ^{13}C NMR ($CDCl_3$, 22.6 Hz) δ 29.9 (C-4), 30.3 (C-1), 43.4 (C-3), (Ar) 124.3, 127.6, 127.9, 130.6, 132.8, 140.3, 207.3 (C-2). Semicarbazone: mp 177.5–179.5 °C (lit.[35] mp 187–188 °C).

B. Acetoacetic Ester Synthesis. Sodium (3.45 g, 150 mmol) was dissolved in 75 mL of EtOH. At 50 °C, 19.5 g (150 mmol) of ethyl acetoacetate was added. After 1 h, 25.5 g (102 mmol) of 2-bromobenzyl bromide was added in one portion (exothermic reaction). The mixture was stirred 0.5 h whereupon an additional 15.7 g (63 mmol) of 2-bromobenzyl bromide was added and stirring was continued for 3 h. Ethanol was removed under reduced pressure, and the mixture was treated with 150 mL of water and 150 mL of Et_2O. After neutralization of the aqueous layer with 1 N hydrochloric acid, the ether layer was separated, washed with brine, dried over Na_2SO_4, and concentrated. Distillation gave 24.5 g (55%) of keto ester **14**: bp 125–135 °C (0.5 mm); ^1H NMR (CCl_4, 60 MHz) δ 1.21 (t, 3 H, CH_2CH_3, J = 7 Hz), 2.21 (s, 3 H, CH_3), 3.3 (m, 2 H, $ArCH_2$), 3.7–3.9 (m, 1 H, CH), 4.10 (q, 2 H, OCH_2), 7.0–7.7 (m, 4 H, Ar)). The keto ester was then stirred with 100 mL of 5% NaOH for 3.5 h at 25 °C. After standing for 0.5 h, the solution phase was decanted from a small quantity of an insoluble oil. The solution was acidified with 10.2 mL of 12 N hydrochloric acid, which was added in small portions. When CO_2 evolution had ceased, the solution was adjusted to pH 3 and the mixture was extracted with several portions of Et_2O that were combined, washed with brine, and dried over Na_2SO_4. Concentration and distillation gave 13.4 g (74%) of **12**.

Ethyl 7-(2-Bromophenyl)-5-methyl-3-oxo-2-(triphenylphosphoranylidene)-4-heptenoate (13). A mixture of 15 mmol of NaH, three drops of 2-propanol, and 7.89 g (15 mmol) of **15** was stirred for 15 min and treated with 2.33 g (10.3 mmol) of ketone **12**. The mixture was allowed to stand overnight whereupon the solvent was removed under reduced pressure and the residue partitioned between CH_2Cl_2 and water. The dried extract (Na_2SO_4) was concentrated and the residue chromatographed on a 24 × 6 cm column of silica gel. Elution with CH_2Cl_2 followed in turn by 10:1 CH_2Cl_2–EtOAc and 3:1 CH_2Cl_2–EtOAc gave 5.83 g (94%) of olefinic ylide **13** as a mixture of *E* and *Z* (7:3) isomers. The *E* isomer, obtained from early chromatographic fractions, crystallized from EtOAc–hexane: mp 121–131 °C: IR ($CHCl_3$) ν 3000, 1650, 1647, 1430, 1362, 1300, 1100, 1084 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 0.68 (t, 3 H, OCH_2CH_3, J = 8 Hz), 1.97 (s, 3 H, CH_3), 2.26–2.52 (m, 2 H, allylic CH_2), 2.83–3.05 (m, 2 H, $ArCH_2$), 3.73 (q, 2 H, OCH_2), 6.95–7.90 (m, 20 H, Ar and CHCO); ^{13}C NMR ($CDCl_3$, 22.6 MHz) δ 13.8 (OCC), 19.1 5-Me), 34.9 (C-6), 41.0 (C-7), 58.3 (OC), 72.6 (d, $^1J_{CP}$ = 111.8 Hz, C-2), (Ph_3P) 127.3 (d, $^1J_{CP}$ = 91.2 Hz), 128.4 (d, $^2J_{CP}$ = 13.2 Hz), 131.4 (d, $^3J_{CP}$ = 10.3 Hz), (Ar) 124.3, 127.4, 128.1, 130.4, 132.8, 141.5, 125.4 (d, $^3J_{CP}$ = 8.8 Hz, C-4), 147.3 (C-5), 167.8 (d, $^2J_{CP}$ = 14.7 Hz, C-1), 189.5 (d, $^2J_{CP}$ = 4.4 Hz, C-3). Anal. Calcd for $C_{34}H_{32}BrO_3P$: C, 68.12; H, 5.38. Found: C, 67.99; H, 5.47.

Reaction of 10 with *n*-BuLi. (a) With 1 equiv. A solution containing 395 mg (0.68 mmol) of **10** in 8 mL THF was cooled to −78 °C and with vigorous stirring was treated with 0.44 mL (0.68 mmol) of 1.55 N *n*-BuLi over 40 s. The mixture was stirred for 3 min and then was quenched by the addition of 100 μL of HOAc. The solvent was removed under reduced pressure, and the residue was treated with water and extracted with CH_2Cl_2. PTLC (silica gel, 20:1 CH_2Cl_2–EtOAc) gave 333 mg (77%) of **61** as an oil: ^1H NMR ($CDCl_3$, 90 MHz) δ 0.65 (t, 3 H, OCH_2CH_3, J = 7.1 Hz), 0.86 (t, 3 H, CH_3), 1.1–3.1 (br, 13 H, CH_2 and CH), 3.72 (q, 2 H, OCH_2), 6.8–7.8 (br, 19 H, aromatic); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 13.8 (CH_3), 14.1 (CH_3), 23.1, 28.8, 33.4, 33.6, 34.4, 34.8, 44.3 (d, $^3J_{CP}$ = 5.4 Hz, C-4), 58.2 (OCH_2), 71.9 (d, $^1J_{CP}$ = 110.1 Hz, C-2), 127.1 (d, $^1J_{CP}$ = 92.1 Hz, Ph), 128.3 (d, $^2J_{CP}$ = 12.1 Hz, Ph), 131.3 (d, $^4J_{CP}$ = 2.7 Hz, Ph), 133.0 (d, $^3J_{CP}$ = 9.4 Hz, Ph), (aryl) 128.3, 127.0, 127.2, 130.3, 132.5 and 142.8, 167.8 (d, $^2J_{CP}$ = 16.1 Hz, C-1), 197.2 (d, $^2J_{CP}$ = 2.7 Hz, C-3).

(b) With 2 equiv. A solution containing 192 mg (0.33 mmol) of ylide **10** in 2 mL of THF was added with stirring to a −78 °C solution containing 0.61 mmol (2 equiv) of *n*-BuLi (hexane) in 5 mL of THF. After 10 min, 0.5 mL of 6.4% aqueous NH_4Cl was added and the mixture was allowed to warm to 20 °C. The residue obtained upon removal of the solvent was extracted with 3:1 Et_2O–CH_2Cl_2, and the extracts were washed with water and brine and dried over Na_2SO_4. Concentration gave an oil that, upon purification by PTLC (silica gel, 8:1 CH_2Cl_2–EtOAc), afforded 130 mg (70%) of ethyl 3-oxo-5-(2-phenylethyl)-2-(triphenylphosphoranylidene)nonanoate (**62**) as a viscous oil: ^1H NMR ($CDCl_3$, 60 MHz) δ 0.61 (t, 3 H, OCH_2CH_3, J = 7 Hz), 0.85 (t, 3 H, CH_3), 1.0–3.0 (br, 13 H, CH_2 and CH), 3.63 (q, 2 H, OCH_2), 7.09 (s, 5 H, Ph), 7.0–7.8 (m, 15 H, Ph). This material was identical by TLC and ^1H NMR spectrum with an authentic sample prepared[15] by the addition of *n*-BuLi to ethyl 3-oxo-7-phenyl-2-(triphenylphosphoranylidene)-4(*E*)-heptenoate.[16]

Reaction of 13 with *n*-BuLi. A solution containing 1.87 mmol of *n*-BuLi in 3 mL of THF was stirred at −78 °C, and a solution of 486 mg (0.81 mmol) of **13** in 3 mL of THF was added quickly. After 20 min the mixture was treated with 0.5 mL of water and allowed to warm to 20 °C. The solvent was removed under reduced pressure, and the residue was extracted with 2:1 CH_2Cl_2–Et_2O. The extract was washed with water and brine and dried over Na_2SO_4. Concentration and purification by PTLC (silica gel, 8:1 CH_2Cl_2–EtOAc) gave 415 mg (98%) of an inseparable 2.5:1 mixture of **64** and **65**. The mixture cold be somewhat enriched in **64** by repeated recrystallization from cold EtOAc, but it could not be completely purified; mp 135–141 °C. Spectral

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properties of the two components were determined from spectra taken using different fractions. **64**: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.62 (t, 3 H, OCH_2CH_3, J = 7.3 Hz), 1.30 (s, 3 H, CH_3), 1.74 (dt, 1 H, $CHHCH_2$, J = 12.4, 7.2 Hz), 2.67–2.85 (m, 3 H, $CHHCH2$), 3.24 (s, 2 H, CH_2CO), 3.65 (q, 2 H, OCH_2), 7.10–7.75 (m, 15 H, Ph). **65**: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.65 (t, 3 H, OCH_2CH_3, J = 7.3 Hz), 2.22–2.50 (m, 4 H, CH_2), 3.72 (q, 2 H, OCH_2), 3.75 (s, 2 H, CH_2CO), 4.86 (br d, 2 H, C=CH_2), 7.1–7.7 (m, 15 H, Ph). An authentic sample of this isomer having the same ^{1}H NMR spectrum was prepared from ethyl 5-methyl-3-oxo-7-phenyl-2-(triphenylphosphoranylidene)-4-heptenoate (a mixture of isomers prepared by Horner–Wittig olefination[16] of 4-phenyl-2-butanone) by deprotonation[15] with n-BuLi in THF at −78 °C (10 min) followed by the kinetic quenching of the allylic anion formed with water. Anal. (isomeric mixture) Calcd for $C_{34}H_{33}O_3P$: C, 78.44; H, 6.39. Found: C, 78.21; H, 6.41.

5,5-Dimethoxy-1-iodo-1(*Z*)-pentene (17). 3-Bromopropanal dimethyl acetal[36] (5.49 g, 30 mmol) was stirred with 0.80 g (32 mmol) of magnesium turnings in 100 mL of THF at 25 °C until Grignard reagent formation was complete (approximately 1.5 h). This solution was added slowly by cannula to a stirred mixture of 6.2 g (30 mmol) of Me_2S–CuBr[37] in 30 mL of Et_2O maintained at −50 °C. After 1 h, the temperature of the mixture was adjusted to −40 °C and approximately 107 mmol of gaseous acetylene (purified by passage through two −78 °C traps) was introduced over 20 min into the mixture just above the solution surface. When the addition was complete, the temperature of the mixture was allowed to rise slowly to −20 °C over 45 min whereupon it was again cooled to −50 °C and treated with 30 mL of HMPA followed by 7.6 g (30 mmol) of iodine. The mixture was slowly warmed to 0 °C over 1 h and then poured into a solution containing 10 g of NH_4Cl and 10 g of NaCN in 100 mL of water. The mixture was thoroughly extracted with 2:1 pentane–ether. Distillation of the dried extracts gave 3.25 g (42%) of pure **17**: bp 68–70 °C (0.05 mm); IR (neat) ν 2960, 2840, 1610, 1120, 1060 cm^{-1}; ^{1}H NMR ($CDCl_3$, 100 MHz) δ 1.60–1.86 (m, 2 H, CH_2CH), 2.10–2.34 (m, 2 H, allylic CH_2), 3.34 (s, 6 H, OCH_3), 4.38 (t, 1 H, CH, J = 6 Hz), 6.25 (s, 2 H, CH=CHI); ^{13}C NMR ($CDCl_3$, 22.6 MHz) δ 20.1 (C-2), 30.8 (C-3), 52.8 (OCH_3), 82.8 (C-5), 103.8 (C-1), 140.3 (C-4). Anal. Calcd for $C_7H_{13}IO_2$: C, 32.83; H, 5.12. Found: C, 32.72; H, 5.14.

5-Iodo-4(*Z*)-pentenal (18). Acetal **17** (1.0 g, 3.9 mmol) was stirred in 30 mL of 50% HOAc for 14 h. Water (25 mL) and brine (10 mL) were added, and the mixture was thoroughly extracted with pentane. The extracts were washed twice with saturated $NaHCO_3$, dried over Na_2SO_4, and concentrated by distillation at ambient pressure. Removal of the remaining solvent at 20 mm pressure gave 950 mg (91%) of **18**, which was used without further purification: IR (neat) ν 2825, 2730, 1717, 1610, 1280 cm^{-1}; ^{1}H NMR (CCl_4, 60 MHz) δ 2.38–2.75 (m, 4 H, CH_2), 6.15–6.62 (m, 2 H, CH=CH), 9.97 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 22.6 MHz) δ 27.6 (C-3), 42.0 (C-2), 84.0 (C-5), 139.0 (C-4), 200.6 (C-1). (2,4-Dinitrophenyl)hydrazone: mp 116.5–117.5 °C. Anal. Calcd for $C_{11}H_{11}IN_4O_4$: C, 33.87; H, 2.84; N, 14.36. Found: C, 34.01; H, 2.96; N, 14.26.

Ethyl 9-Iodo-3-oxo-2-(triphenylphosphoranylidene)-4-(*E*),8(*Z*)-nonadienoate (19). A solution containing 573 mg (2.73 mmol) of aldehyde **18** in 2 mL of THF was added to a stirred mixture of 3.1 mmol of NaH, 1.58 g (3.0 mmol) of **15**, and 3 drops of EtOH in 10 mL of THF. After 45 min, the solution phase was decanted from the gummy phosphate deposits that were further extracted with CH_2Cl_2. The combined organic phases were concentrated in vacuo, and the residue was chromatographed on a 5 × 20 cm column of silica gel. Elution with 10:1 CH_2Cl_2–EtOAc gave 1.55 g (97%) of crude **19**, >90% pure by NMR analysis. Crystallization from EtOAc–hexane gave pure **19**: mp 93–94 °C; IR ($CHCl_3$) ν 3000, 1655, 1640, 1437, 1372, 1294, 1100, 1088 cm^{-1}; ^{1}H NMR ($CDCl_3$, 60 MHz) δ 0.67 (t, 3 H, OCH_2CH_3, J = 7 Hz), 2.30 (m, 4 H, CH_2), 3.72 (q, 2 H, OCH_2), 6.15 (m, 2 H, CH=CHI), 6.2–6.8 (m, 1 H, CHCO), 7.2–7.9 (m, 16 H, Ar and CH=CHCO); ^{13}C NMR ($CDCl_3$, 22.6 MHz) δ 13.6 (OCC), 30.6 (C-7), 33.8 (C-6), 58.4 (OC), 71.7 (d, $^1J_{CP}$ = 111.5 Hz, C-2), 82.7 (C-9), 127.0 (d, $^1J_{CP}$ = 92.7 Hz, Ph), 128.4 (d, $^2J_{CP}$ = 13.4 Hz, Ph), 129.5 (d, $^3J_{CP}$ = 9.4 Hz, C-4), 131.4 (d, $^4J_{CP}$ = 4.0 Hz, Ph), 133.0 (d, $^3J_{CP}$ = 10.8 Hz, Ph), 139.3 (C-5), 140.4 (C-8), 167.6 (d, $^2J_{CP}$ = 14.8 Hz, C-1), 186.4 (d, $^2J_{CP}$ = 4.0 Hz, C-3). Anal. Calcd for $C_{29}H_{28}IO_3P$: C, 59.80; H, 4.85. Found: C, 59.97; H, 5.01.

Cyclization of 19 with *n*-BuLi. To a stirred solution containing 300 mg (0.52 mmol) of **19** in 5 mL of THF at −78 °C was slowly added 1.14 mmol of n-BuLi in hexane. After 15 min, 0.2 mL of water was added and the mixture was allowed to warm to 20 °C whereupon the solvent was removed under reduced pressure. Purification of the residue by PTLC (8:1 CH_2Cl_2–EtOAc) gave 204 mg (87%) of cyrstalline **66**. An analytical sample was obtained by recrystallization from EtOAc–hexane: mp 120–121 °C; IR ($CHCl_3$) ν 3000, 1650, 1640, 1430, 1365, 1290, 1098, 1085 cm^{-1}; ^{1}H NMR ($CDCl_3$, 89.5 MHz) δ 0.65 (t, 3 H, OCH_2CH_3, J = 7.0 Hz), 1.2–2.4 (m, 4 H, ring CH_2), 2.8–3.0 (m, 2 H, CH_2CO), 3.0–3.2 (m, 1 H, CH), 3.73 (q, 2 H, OCH_2), 5.66 (s, 2 H, CH=CH), 7.3–7.8 (m, 15 H, Ph); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 13.8 (OCC), 29.7 (C-4′), 31.9 (C-5′), 42.7 (C-3′), 46.2 (d, $^3J_{CP}$ = 6.7 Hz, C-4), 58.2 (OC), 73.8 (d, $^1J_{CP}$ = 110.1 Hz, C-2), 127.2 (d, $^1J_{CP}$ = 94.0 Hz, Ph), 128.3 (d, $^2J_{CP}$ 13.4 Hz, Ph), 129.7 (C-2′), 131.4 (d, $^4J_{CP}$ = 2.7 Hz, Ph), 133.1 (d, $^3J_{CP}$ = 10.7 Hz, Ph), 135.8 (C-1′), 167.8 (d, $^2J_{CP}$ = 14.0 Hz, C-1), 197.0 (d, $^2J_{CP}$ = 2.7 Hz, C-3). Anal. Calcd for $C_{29}H_{29}O_3P$: C, 76.30; H, 6.40. Found: C, 76.13; H, 6.18.

Hydrogenation of this product (1 atm H_2, PtO_2, EtOAc, 0.5 h) gave **78** (96%; mp and mixed mp 116–118 °C) identical with an authentic sample:[23] ^{1}H NMR ($CDCl_3$, 60 MHz) δ 0.67 (t, 3 H, OCH_2CH_3, J = 7 Hz), 1.0–2.6 (br, 9 H, ring CH_2 and CH), 2.8–3.1 (m, 2 H, CH_2O), 3.73 (q, 2 H, OCH_2), 7.3–8.0 (m, 15 H, Ph); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 13.8 (OCC), 25.1 (C-3′), 32.6 (C-2′), 37.0 (C-1′), 46.1 (d, C-4, $^3J_{CP}$ = 5.4 Hz), 58.2 (OC) 71.3 (d, C-2, $^1J_{CP}$ = 110.1 Hz), 127.3 (d, Ph, $^1J_{CP}$ = 94.0 Hz), 128.3 (d, Ph, $^2J_{CP}$ = 12.1 Hz), 131.3 (d, Ph, $^4J_{CP}$ = 2.7 Hz), 133.0 (d, Ph, $^3J_{CP}$ = 9.4 Hz), 167.8 (d, C-1, $^2J_{CP}$ = 16.1 Hz), 197.7 (d, C-3, $^2J_{CP}$ = 4.0 Hz).

Cyclization and Alkylation of 19 with *t*-BuLi. (a) A stirred solution containing 140 mg (0.24 mmol) of **19** in 3 mL of THF was cooled to −78 °C and treated dropwise over 4 min with 0.55 mmol of t-BuLi in pentane. This mixture was stirred for 40 min, then treated with 40 μL (0.33 mmol) of benzyl bromide, and allowed to warm to 20 °C. After 2.5 h at 20 °C, several drops of H_2O were added and the mixture was concentrated, treated with H_2O, and extracted with CH_2Cl_2. The extracts were washed with water, dried (Na_2SO_4), and concentrated. Chromatography of the residue (PTLC, 12:1 CH_2Cl_2–EtOAc) gave 119 mg (91%) of **67** as a thick oil (a mixture of diastereomers) that slowly crystallized: ^{1}H NMR ($CDCl_3$, 89.5 MHz) δ 0.62 (t, 3 H, OCH_2CH_3, J = 7.1 Hz), 1.4–2.4 (br, 4 H, CH_2), 2.5–3.2 (br, 3 H, benzylic CH_2, allylic CH), 3.63 (q, 2 H, OCH_2), 4.46 (m, 1 H, CHCO, 5.73 (s, 2 H, CH=CH), 7.20 (s, 5 H, Ph), 7.25–7.60 (m, 15 H, PhP). Crystallization of the mixture from EtOAc–hexane gave an analytical sample, mp 123–124 °C. Anal. Calcd for $C_{36}H_{35}O_3P$: C, 79.10; H, 6.45. Found: C, 79.20; H, 6.60.

(b) A solution containing 200 mg (0.34 mmol) of **19** in 3 mL of THF was stirred at −78 °C while 0.73 mmol of t-BuLi in pentane was added over 5 min. The mixture was stirred for 40 min, treated with 45 μL (0.48 mmol) of methyl bromoacetate, and then heated at 55 °C for 1 h. After the addition of a small amount of water, solvents were removed in vacuo and the residue was partitioned between water and CH_2Cl_2. Concentration of the dried organic phase gave a residue that upon chromatography (PTLC, 10:1 CH_2Cl_2–EtOAc) gave 120 mg (67%) of **68** (R_f 0.4) as a thick oil (mixture of diastereomers): IR ($CHCl_3$) 3000, 1728, 1650, 1655, 1548, 1436, 1295, 1100, 1090 cm^{-1}; ^{1}H NMR ($CDCl_3$, 89.5 MHz) δ 0.66, 0.67 (2 t, 3 H, OCH_2CH_3), 1.35–1.85 (br, 2 H, CH_2), 1.85–2.45 (br, 4 H, CH_2), 2.5–3.0 (m, 1 H, CH), 3.52, 3.54 (2 s, 3 H, OCH_3), 3.73, 3.74 (2 q, 2 H, OCH_2), 4.38 (m, 1 H, CHCO), 5.4–5.8 (m, 2 H, CH=CH), 7.2–7.8 (m, 15 H, PhP). Additionally, 60 mg (32%) of an unstable halogen-containing compound was obtained (R_f 0.7), which is thought to be **69** on the basis of a multiplet at 5.3 ppm in its complex ^{1}H NMR spectrum. Reduction of this material (50 mg) by heating with 75 mg of Ph_3P in 0.3 mL of EtOH at reflux for 1 h gave, after PTLC, 26 mg (61%) of **66**.

6-Iodo-5(Z)-hexen-2-ol (20). A solution of 2.35 g (11.2 mmol) of 5-iodo-4(*Z*)-pentenal (**18**) in 10 mL of THF was added dropwise to a stirred 0 °C solution of 12.1 mmol of MeMgBr (2.9 M in Et_2O) in 35 mL of THF. After 15 min the mixture was allowed to warm

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to 20 °C whereupon 12 mL of 1 N HCl was added. The mixture was partitioned between 50% saturated NaCl and 1:1 pentane–Et_2O. Concentration of the organic phase gave 2.3 g (91%) of **20**, >95% pure, which was used without further purification. An analytical sample was prepared by distillation: bp 75–80 °C (1.5 mm); IR (neat) ν 3360, 2965, 2925, 1603, 1370, 1290, 1278, 1120, 1070 cm^{-1}; ^1H NMR ($CDCl_3$, 89.5 MHz) δ 1.22 (d, 2 H, CH_3, J = 6.4 Hz), 1.4–1.7 (m, 2 H, CH_2CH), 2.1–2.4 (m, 2 H, allylic CH_2), 2.47 (s, 1 H, OH), 3.82 (m, 1 H, CH), 6.06–6.33 (m, 2 H, CH=CHI); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 23.4 (C-1), 31.2 (C-4), 37.1 (C-3), 67.2 (C-2), 82.6 (C-6), 140.8 (C-5). Anal. Calcd for $C_6H_{11}OI$: C, 31.88; H, 4.90. Found: C, 31.97; H, 4.89.

6-Iodo-5(*Z*)-hexen-2-one (21). Alcohol **20** (2.0 g, 8.8 mmol) was added with stirring to 2.88 g (13.4 mmol) of pyridinium chlorochromate in 20 mL of CH_2Cl_2. After the mixture was stirred for 2 h, 60 mL of Et_2O was added and the solution phase was decanted from the gummy residue. Filtration of this solution through a short plug of silica gel followed by removal of the solvent gave 1.11 g (56%) of ketone **21**, which was >96% pure. An analytical sample was prepared by bulb-to-bulb distillation (140 °C, 1.0 mm): IR ($CHCl_3$) ν 2910, 1707, 1605, 1360, 1280, 1152 cm^{-1}; ^1H NMR ($CDCl_3$, 89.5 MHz) δ 2.16 (s, 3 H, CH_3), 2.3–2.7 (m, 4 H, CH_2), 6.15–6.35 (m, 2 H, CH=CHI); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 29.0 (C-1), 29.8 (C-4), 41.5 (C-3), 83.5 (C-5), 139.6 (C-5), 139.6 (C-5), 207.2 (C-2). Anal. Calcd for C_6H_9IO: C, 32.17; H, 4.05. Found: C, 32.09; H, 4.23.

Ethyl 9-Iodo-5-methyl-3-oxo-2-(triphenylphosphoranylidene)-4(*E*/*Z*),8(*Z*)-nonadienoate (22). In the manner previously described for the preparation of **13**, 247 mg (1.1 mmol) of **21**, upon treatment with 1.5 mmol of NaH and 790 mg (1.5 mmol) of **15** for 1.5 h, gave 215 mg (33%) of noncrystalline **22** as a mixture of isomers (4-*E*:4-*Z* ≈ 3:1) after PTLC (double development, 20:1 and 15:1 CH_2Cl_2–EtOAc): IR ($CHCl_3$) ν 3000, 1650, 1637, 1480, 1435, 1365, 1300, 1100, 1084 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 0.66 (t, 3 H, CH_3CH_2O, J = 7 Hz), 1.88 (br s, 3 H, CH_3), 2.1–2.6 (m, 4 H, CH_2), 3.67 (q, 2 H, OCH_2), 6.0 (m, 2 H, CH=CHI of minor isomer), 6.18 (br s, 2 H, CH=CHI of major isomer), 7.0 (br s, 1 H, CHCO), 7.15–7.90 (m, 15 H, Ph); ^{13}C NMR ($CDCl_3$, 22.5 MHz) (E-isomer) δ 13.9 (OCC), 18.8 (5-Me), 33.0 (C-7), 38.7 (C-6), 58.3 (OC), 72.3 (d, $^1J_{CP}$ = 111.5 Hz, C-2), 82.4 (C-9), 125.9 (d, $^3J_{CP}$ = 9.4 Hz, C-4), 127.3 (d, $^1J_{CP}$ = 94.0 Hz, Ph), 128.4 (d, $^2J_{CP}$ = 13.4 Hz, Ph), 131.4 (d, $^4J_{CP}$ = 2.7 Hz, Ph), 133.2 (d, $^3J_{CP}$ = 9.4 Hz, Ph), 140.8 (C-8), 146.4 (C-5), 167.5 (d, $^2J_{CP}$ = 14.8 Hz, C-1), 189.5 (d, $^2J_{CP}$ = 4.0 Hz, C-3).

Cyclization of 22 with *n*-BuLi. To a −78 °C solution containing 213 mg (0.36 mmol) of *E*/*Z*-**22** in 5 mL of THF was added slowly, with stirring, 0.91 mmol of *n*-BuLi (1.5 N in hexane). After 15 min, 0.2 mL of water was added and the mixture was allowed to warm to 20 °C. Solvent evaporation followed by PTLC (8:1 CH_2Cl_2–EtOAc) gave 157 mg (93%) of **70**: mp 135–136 °C (EtOAc–hexane); IR ($CHCl_3$) ν 3000, 1655, 1648, 1438, 1370, 1295, 1100, 1085 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.67 (t, 3 H, OCH_2CH_3), 1.08 (s, 3 H, CH_3), 1.6–2.3 (m, 4 H, CH_2), 2.79 and 3.18 (q, 2 H, CH_2CO, J_{AB} = 14 Hz), 5.34–5.69 (m, 2 H, olefinic), 7.1–7.9 (m, 15 H, Ph); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 13.8 (OCC), 27.3 (3′-CH_3), 31.3 (C-4′), 36.9 (C-5′), 48.7 (d, C-4, $^3J_{CP}$ = 6.0 Hz), 48.7 (C-3′), 73.1 (d, C-2, $^1J_{CP}$ = 110.1 Hz), 127.3 (d, Ph, $^1J_{CP}$ = 92.7 Hz), 127.5 (C-2′), 128.3 (d, Ph, $^2J_{CP}$ = 13.4 Hz), 131.3 (d, Ph, $^4J_{CP}$ = 2.7 Hz), 133.0 (d, Ph, $^3J_{CP}$ = 9.4 Hz), 141.1 (C-1′), 167.8 (d, C-1, $^2J_{CP}$ = 16.1 Hz), 196.4 (d, C-3, $^2J_{CP}$ = 3.3 Hz). Anal. Calcd for $C_{30}H_{31}O_3P$: C, 76.58; H, 6.64. Found: C, 76.72; H, 6.70.

6-Iodo-5-hexen-1-ol (25). Magnesium turnings (3.0 g, 0.12 mol) in 25 mL of Et_2O were activated by the addition of 500 μL of ethylene dibromide. After cessation of gas evolution, the Et_2O was removed by cannula and replaced with 20 mL of THF and 10 mL of Et_2O. A solution of 7.30 g (37.9 mmol) of 2-(4-chlorobutoxy)tetrahydro-2*H*-pyran (**23**)[38] and 500 μL of ethylene dibromide in 10 mL of THF was added rapidly with stirring When gas evolution and refluxing ceased, the mixture was allowed to stand with occasional stirring for 1 h. The solution of Grignard reagent was added over 10 min to a stirred slurry of 8.0 g (39 mmol) of Me_2S–CuBr in 15 mL of THF maintained at −40 to −50 °C. The mixture was stirred at −50 °C for 1 h whereupon acetylene was passed into the flask over 20 min at a rate of approximately 200 mL/min. (The temperature was allowed to rise to −25 °C during the addition, and acetylene introduction was discontinued when no further absorption was noted at this temperature.) The mixture was cooled to −50 °C, and 30 mL of HMPA was added. After warming to −35 °C, a solution containing 9.6 g (38 mmol) of iodine in 15 mL of THF was added and the mixture was allowed to warm to 5 °C over 30 min. The mixture was poured into 100 mL of a freshly prepared 10% solution of 1:1 NaCN–NH_4Cl and thoroughly extracted with 1:1 Et_2O–pentane. The extracts were washed with water and brine and dried over Na_2SO_4. Solvent removal gave 11.4 g of crude product, which upon distillation gave 2.5 g of a mixture of **25** and its THP ether **24**: bp 90–103 °C (0.05 mm). This mixture was stirred in 50 mL of 60% HOAc for 3 h followed by the addition of 50 mL of water and extraction with Et_2O–pentane. Solvent evaporation and PTLC (8:1 CH_2Cl_2–EtOAc) gave 1.90 g (22% overall) of pure **25**: IR (neat) ν 3330, 2930, 1606, 1270, 1060 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 1.57 (m, 4 H, CH_2), 2.16 (m, 2 H, allylic CH_2), 3.59 (t, 2 H, CH_2O), 3.78 (s, 1 H, OH), 6.17 (s, 2 H, CH=CHI); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 24.2 (C-3), 32.1 (C-2), 34.4 (C-4), 62.6 (C-1), 82.6 (C-6), 140.9 (C-5). An analytical sample was obtained by bulb-to-bulb distillation (120°C, 0.5 mm). Anal. Calcd for $C_6H_{11}IO$: C, 31.88; H, 4.91. Found: C, 31.74, H, 4.94.

6-Iodo-5(*Z*)-hexenal (26). Alcohol **25** (1.50 g, 6.64 mmol) was added to a stirred mixture of 1.0 g (4.64 mmol) of pyridinium chlorochromate in 100 mL of CH_2Cl_2. After 1 h, 100 mL of Et_2O was added and the mixture was filtered through a short plug of silica gel. Evaporation and PTLC (9:1 CH_2Cl_2–EtOAc) gave 1.06 g (71%) of **26** suitable for use without distillation: IR (neat) ν 2920, 1723, 1610 cm^{-1}; ^1H NMR ($CDCl_3$, 89.5 MHz) δ 1.5–2.0 (m, 2 H, CH_2), 2.00–2.35 (m, 2 H, allylic CH_2), 2.35–2.60 (m, 2 H, CH_2CO), 6.02–6.35 (m, 2 H, CH=CHI), 9.79 (t, 1 H, CHO, J = 1.5 Hz); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 20.4 (C-3), 33.9 (C-4), 42.9 (C-2), 83.6 (C-6), 140.0 (C-5), 201.6 (C-1). (2,4-Dinitrophenyl)-hydrazone: mp 101–102 °C. Anal. Calcd for $C_{12}H_{13}IN_4O_4$: C, 35.66; H, 3.24; N, 13.86. Found: C, 35.64; H, 3.30; N, 13.65.

Ethyl 10-Iodo-3-oxo-2-(triphenylphosphoranylidene)-4-(*E*),9(*Z*)-decadienoate (27). In the manner described above for the preparation of **10**, 947 mg (1.8 mmol) of **26** gave 787 mg (78%) of **27** after purification by PTLC (8:1 CH_2Cl_2–EtOAc): mp 88–89 °C; IR ($CHCl_3$) ν 3000, 1652, 1642, 1366, 1286, 1100, 1085 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 0.66 (t, 3 H, CH_3, J = 7 Hz), 1.4–1.8 (m, 2 H, CH_2), 2.0–2.4 (m, 4 H, allylic CH_2), 3.76 (q, 2 H, OCH_2), 6.22 (s, 2 H, CH=CHI), 6.68 (dt, 1 H, CHCO, J = 16, 7 Hz), 7.4–8.0 (m, 16 H, Ph and C*H*=CHCO); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 13.7 (OCC), 26.9 (C-6), 31.7 (C-7), 34.3 (C-5), 58.3 (OC), 71.5 (d, C-2, $^1J_{CP}$ = 111.5 Hz), 82.4 (C-9), 127.0 (d, Ph, $^1J_{CP}$ = 94.0 Hz), 128.4 (d, Ph, $^2J_{CP}$ = 12.1 Hz), 129.1 (d, C-3, $^3J_{CP}$ = 9.4 Hz), 131.4 (d, Ph, $^4J_{CP}$ = 2.7 Hz), 133.0 (d, Ph, $^3J_{CP}$ = 9.4 Hz), 140.3 (C-4), 140.9 (C-8), 167.6 (d, C-1, $^2J_{CP}$ = 14.8 Hz), 186.6 (d, C-3, $^2J_{CP}$ = 4.0 Hz). Anal. Calcd for $C_{30}H_{30}IO_3P$: C, 60.41; H, 5.07. Found: C, 60.70; H, 5.10.

Cyclization of 27 with *n*-BuLi. A solution of 209 mg (0.35 mmol) of **27** in 3 mL of THF was cooled to −78 °C, and with stirring 0.25 mL (0.38 mmol) of 1.52 N *n*-BuLi in hexane was added dropwise over 4.0 min. Stirring was continued for 10 min whereupon an additional 0.18 mmol of *n*-BuLi solution was added over 2.0 min. The mixture was stirred for an additional 4.0 min and then treated with drops of aqueous THF until the yellow color of the intermediate ylide anion was discharged. After the solution was warmed to 20 °C, the solvent was removed under reduced pressure and the residue was dissolved in CH_2Cl_2 and washed with water. Solvent evaporation followed by PTLC (12:1 CH_2Cl_2–EtOAc) gave 150 mg (91%) of **71** as a viscous oil that crystallized from EtOAc–hexane: mp 115–117 °C; IR ($CHCl_3$) ν 3000, 2940, 1652, 1642, 1432, 1370, 1300, 1100, 1088 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 0.66 (t, 3 H, OCH_2CH_3, J = 7.2 Hz), 1.05–2.40 (br, 7 H, CH_2, CH), 2.5–3.1 (br, 2 H, CH_2CO), 3.73 (q, 2 H, OCH_2), 5.60 (s, 2 H, CH=CH), 7.2–8.0 (m, 15H, Ph); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 13.8 (OCC), 21.3 (C-4′), 25.3 (C-5′), 29.1 (C-6′), 32.6 (C-3′), 46.2 (d, C-4, $^3J_{CP}$ = 6.7 Hz), 58.3 (OC), 71.6 (d, C-2, $^1J_{CP}$ = 110.1 Hz), 126.3 (C-2′), 127.2 (d, Ph, $^1J_{CP}$ = 94.0 Hz), 128.3 (d, Ph, $^2J_{CP}$ = 13.4 Hz), 131.4 (d, Ph, $^4J_{CP}$ = 2.7 Hz), 132.4 (C-1′), 133.0 (d, Ph, $^3J_{CP}$ = 9.4 Hz), 167.8 (d, C-1, $^2J_{CP}$ = 16.1 Hz) 196.8 (C-3). Anal. Calcd for $C_{30}H_{31}O_3P$: C, 76.57; H, 6.64. Found: C, 76.70; H, 6.72.

(38) Ames, D. E.; Archibald, J. L. *J. Chem. Soc.* **1962**, 1475.

Hydrogenation of this material (H_2, PtO_2, EtOAc, 0.5 h) gave ethyl 4-cyclohexyl-3-oxo-2-(triphenylphosphoranylidene)butanoate (**79**), mp and mixed mp 135.0–137.5 °C, identical with that of the product obtained from **50** (vide infra).

Cyclization and Alkylation of 27 with *t*-BuLi. A solution containing 200 mg (0.34 mmol) of **27** in 3 mL of THF was stirred at −78 °C and treated dropwise over 8 min with 0.73 mmol of *t*-BuLi in pentane. The resulting yellow solution was stirred at −78 °C for 40 min and then treated with 162 μL (2 mmol) of EtI whereupon the mixture was warmed to 55 °C. After 1.5 h at 55 °C the nearly colorless solution was concentrated in vacuo, and the residue was treated with water and extracted with CH_2Cl_2. The dried extract gave, upon concentration and PTLC (15:1 CH_2Cl_2–EtOAc), 17 mg (11%) of **71** and 130 mg (78%) of **72** as mixture of noncrystalline diastereomers (ratio 1.15:1): IR ($CHCl_3$) ν 3000, 2940, 1650, 1538, 1482, 1447, 1378, 1388, 1300, 1100, 907 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ 0.65 (t, 3 H, CH_3, J = 7.1 Hz), 0.66 (t, 3 H, CH_3, J = 7.0 Hz), 0.76 (t, 3 H, CH_3, J = 6.8 Hz), 1.0–2.0 (br, 8 H, CH_2), 2.3–2.8 (br m, 1 H, allylic CH), 3.71 (q, 3 H, OCH_2 and CHCO), 5.5–5.7 (br, 2 H, CH=CH), 7.3–7.8 (m, 15 H, PhP); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 12.0 (C-6), 13.7 (OC*C*), 21.3, 21.6 (C-5), 22.1 (C-5′), 25.3, 25.7 (C-6′), 27.2 (C-4′), 38.0 (C-1′), 50.7, 51.3 (2d, C-4, $^3J_{CP}$ = 5.3, 6.7 Hz), 58.3 (OC), 73.5 (d, C-2, $^1J_{CP}$ = 108.1 Hz), 126.5, 127.0 (C-3′), 127.4 (d, Ph, $^1J_{CP}$ = 92.7 Hz), 128.3 (d, Ph, $^2J_{CP}$ = 12.1 Hz), 130.4 (C-2′), 131.3 (d, Ph, $^4J_{CP}$ = 4.0 Hz), 132.1 (C-2′), 133.0 (d, Ph, $^3J_{CP}$ = 9.4 Hz), 167.5 (d, C-1, $^2J_{CP}$ = 17.5 Hz), 199.3 (C-3).

Ethyl 7-[(2-Tetrahydropyranyl)oxy]-3-oxo-2-(triphenylphosphoranylidene)-4(*E*)-heptenoate (32). To 6.37 g (12.0 mmol) of **15** in 90 mL of THF at −78 °C was slowly added with stirring 4.9 mL (12.7 mmol) of 2.6 M *n*-BuLi. The solution was stirred for 15 min whereupon 2.01 g (12.7 mmol) of **31**[39] in 20 mL of THF was added over 5 min. After 20 min at −78 °C and 15 min at 0 °C, the mixture was poured into 25 mL of water and extracted with ether. The dried extract (Na_2SO_4) was concentrated and upon chromatography (silica gel, 1:1 EtOAc–hexane) gave 4.5 g (71%) of **32** as an oil: ^1H NMR ($CDCl_3$, 90 MHz) δ 0.66 (t, 3 H, OCH_2CH_3, J = 7.1 Hz), 1.57 (br, 6 H, CH_2), 2.5 (m, 2 H, allylic CH_2), 3.35–4.0 (m, 4 H, OCH_2), 3.72 (q, 2 H, OCH_2, J = 7.1 Hz), 4.57 (br, 1 H, OCHO), 6.63 (dt, 1 H, CH_2CH=CH, J = 15.4, 6.8 Hz), 7.3–7.8 (m, 16 H, Ar and CHCO); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 13.7 (OCH_2CH_3), 19.5, 25.5, 30.6, 62.1, 98.5 (THP), 32.8 (C-6), 66.4 (C-7), 71.7 (d, $^1J_{CP}$ = 111.5 Hz, C-2), 130.2 (d, $^3J_{CP}$ = 8.1 Hz, C-4), 137.2 (C-5), 126.6 (d, $^1J_{CP}$ = 94 Hz, Ph), 128.5 (d, $^2J_{CP}$ = 12.1 Hz, Ph), 131.5 (d, $^4J_{CP}$ = 2.7 Hz, Ph), 133 (d, $^3J_{CP}$ = 9.4 Hz, Ph), 1.67 (d, $^2J_{CP}$ = 13.4 Hz, C-1), 186.4 (d, $^2J_{CP}$ = 4.0 Hz, C-3).

Ethyl 7-Hydroxy-3-oxo-2-(triphenylphosphoranylidene)-4(*E*)-heptenoate (33). A solution of 3.61 g (6.8 mmol) of **32** and 0.5 g (2 mmol) of pyridinium *p*-toluenesulfonate in 50 mL of EtOH was heated at 55 °C for 12 h. The solvent was removed under reduced pressure, and the residue was treated with 15 mL of water, made basic with 1 N NaOH, and extracted with ether. Concentration of the dried extracts (Na_2SO_4) followed by chromatography (silica gel, 3:2 EtOAc–CH_2Cl_2 and then 5:1 EtOAc–EtOH) gave 2.53 g (84%) of **33**: mp 145.5 °C (ethyl acetate–hexane); ^1H NMR ($CDCl_3$, 90 MHz) δ 0.64 (t, 3 H, OCH_2CH_3, J = 7.1 Hz), 2.25–2.55 (m, 3 H, CH_2CH_2OH), 3.63 (t, 2 H, CH_2OH, J = 6.8 Hz), 3.72 (q, 2 H, OCH_2), 6.50 (td, 1 H, CH_2CH=CH, J = 6.8, 15.4 Hz), 7.3–7.8 (m, 16 H, Ar and CHCO); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 13.7 (OCH_2CH_3), 35.7 (C-6), 58.5 (OCH_2), 61.3 (C-7), 71.7 (d, $^1J_{CP}$ = 111.5 Hz, C-2), 131.2 (C-4), 136.8 (C-5), 126.7 (d, $^1J_{CP}$ = 91.3 Hz, Ph), 128.5 (d, $^2J_{CP}$ = 13.4 Hz, Ph), 131.5 (d, $^4J_{CP}$ = 4 Hz, Ph), 133.1 (d, $^3J_{CP}$ = 10.7 Hz, Ph), 167.7 (d, $^2J_{CP}$ = 14.8 Hz, C-1), 186.8 (d, $^2J_{CP}$ = 4.0 Hz, C-3). Anal. Calcd for $C_{27}H_{27}O_4P$: C, 72.63; H, 6.10. Found: C, 72.88; H, 6.10.

Ethyl 7-(Mesyloxy)-3-oxo-2-(triphenylphosphoranylidene)-4(*E*)-heptenoate (34). A solution containing 110 mg of **33** in 2 mL of dry pyridine was treated with 0.05 mL (0.6 mmol) of methanesulfonyl chloride and stirred at 20 °C for 40 min. After solvent removal under reduced pressure, the residue was extracted with ether and the extracts were dried (Na_2SO_4) and concentrated. Chromatography of the residue (silica gel, 3:1 EtOAc–CH_2Cl_2) gave 115 mg (89%) of pure **34**. An analytical sample, mp 102 °C, was obtained by recrystallization from ethyl acetate–hexane: ^1H NMR ($CDCl_3$, 90 MHz) δ 0.63 (t, 3 H, OCH_2CH_3, J = 7.1 Hz), 2.63 (q, 2 H, allylic CH_2), 3.0 (s, 3 H, CH_3SO_2), 3.7 (q, 2 H, OCH_2), 4.29 (t, CH_2OSO_2, J = 6.8 Hz), 6.51 (td, 1 H, CH_2CH=CH, J = 16.0, 6.8 Hz), 7.3–7.85 (m, 16 H, Ar and CHCO); ^{13}C NMR ($CDCl_3$, 22.5 Hz) δ 13.7 (OCH_2CH_3), 31.9 (CH_3SO_2), 37.5 (C-6), 58.5 (OCH_2), 68.6 (C-7), 72.1 (d, $^1J_{CP}$ = 111.5 Hz, C-2), 132.1 (C-5), 133.7 (C-4), 126.7 (d, $^1J_{CP}$ = 96.7 Hz, Ph), 128.5 (d, $^2J_{CP}$ = 13.4 Hz, Ph), 131.6 (d, $^4J_{CP}$ = 2.7 Hz, Ph), 133.0 (d, $^3J_{CP}$ = 9.4 Hz, Ph), 167.6 (d, $^2J_{CP}$ = 13.4 Hz, C-1), 185.7 (d, $^2J_{CP}$ = 4.0 Hz, C-3). Anal. Calcd for $C_{28}H_{29}O_6PS$: C, 64.11; H, 5.57. Found: C, 64.31; H, 5.80.

Ethyl 7-Chloro-3-oxo-2-(triphenylphosphoranylidene)-4-(*E*)-heptenoate (35). A solution containing 0.76 g (1.45 mmol) of **34** and 1.2 g (28 mmol) of LiCl in 10 mL of dry DMF was stirred at 25 °C for 8 h, then poured into 10 mL of saturated $NaHCO_3$ solution, and twice extracted with ether (2 × 40 mL). The extracts were washed with brine, dried over $MgSO_4$, and concentrated. Recrystallization of the residue from ethyl acetate–hexane gave 633 mg (94%) of **35**: mp 118 °C; ^1H NMR ($CDCl_3$, 90 MHz) δ 0.65 (t, 3 H, OCH_2CH_3, J = 7.1 Hz), 2.64 (m, 2 H, CH_2CH_2Cl), 3.57 (t, 2 H, CH_2Cl, J = 7.1 Hz), 3.72 (q, 2 H, OCH_2), 6.64 (td, 1 H, $CHCH_2$, J = 15.4, 7.1 Hz), 7.2–7.85 (m, 16 H, Ar and CHCO); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 13.7 (OCH_2CH_3), 35.6 (C-6), 43.1 (C-7), 58.5 (OCH_2), 71.9 (d, $^1J_{CP}$ = 111.5 Hz (C-2), 131.1 (d, $^3J_{CP}$ = 8.1 Hz, C-4), 135.5 (C-5), 126.8 (d, $^1J_{CP}$ = 91.3 Hz, Ph), 128.5 (d, $^2J_{CP}$ = 12.1 Hz, Ph), 131.6 (d, $^4J_{CP}$ = 4 Hz, Ph), 133.0 (d, $^3J_{CP}$ = 9.4 Hz, Ph), 167.6 (d, $^2J_{CP}$ = 14.8 Hz, C-1), 181.1 (d, $^2J_{CP}$ = 4 Hz, C-3). Anal. Calcd for $C_{27}H_{26}ClO_3P$: C, 69.75; H, 5.64. Found: C, 69.81; H, 5.71.

Ethyl 7-Iodo-3-oxo-2-(triphenylphosphoranylidene)-4-(*E*)-heptenoate (36). A solution containing 209 mg (0.4 mmol) of **35** and 1.2 g (8 mmol) of NaI in 10 mL of acetone was stirred for 12 h at 25 °C and then concentrated under reduced pressure. The residue was extracted with ether (2 × 30 mL), and the extracts were washed with brine, dried ($MgSO_4$), and concentrated. Recrystallization of the residue from ethyl acetate–hexane gave 224 mg (100%) of **36**: mp 101–102 °C; ^1H NMR ($CDCl_3$, 90 MHz) δ 0.65 (t, 3 H, OCH_2CH_3, J = 7.1 Hz), 2.76 (m, 2 H, allylic CH_2), 3.19 (t, 2 H, CH_2I, J = 6.8 Hz), 3.72 (q, 2 H, OCH_2), 6.48 (td, 1 H, CH_2CH=CH, J = 15.6, 6.7 Hz), 7.3–7.8 (m, 16 H, Ar and CHCO); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 2.9 (C-7), 13.7 (CH_3), 36.7 (C-6), 58.5 (OCH_2), 71.9 (d, $^1J_{CP}$ = 111.5 Hz, C-2), 130.5 (d, $^3J_{CP}$ = 8.1 Hz, C-4), 138.0 (C-5), 126.7 (d, $^1J_{CP}$ = 92.6 Hz, Ph), 128.5 (d, $^2J_{CP}$ = 12.1 Hz, Ph), 131.5 (d, $^4J_{CP}$ = 12.1 Hz, Ph), 131.5 (d, $^4J_{CP}$ = 2.7 Hz, Ph), 133.0 (d, $^3J_{CP}$ = 9.4 Hz, Ph), 167.6 (d, $^2J_{CP}$ = 14.8 Hz, C-1), 186.0 (d, $^2J_{CP}$ = 4.0 Hz, C-3). Anal. Calcd for $C_{27}H_{26}IO_3P$: C, 58.29; H, 4.71. Found: C, 58.49; H, 4.92.

Cyclization of 36 with *n*-BuLi. A solution containing 99 mg (0.18 mmol) of **36** in 3 mL of THF was cooled to −78 °C and with vigorous stirring treated slowly with 1.4 mL (2.1 mmol) of 1.5 M *n*-BuLi. After 15 min at −78 °C, the mixture was kept at 20 °C for 10 min, then poured into 10 mL of water, and extracted with ether. Concentration of the dried extracts (Na_2SO_4) followed by chromatography of the residue (silica gel, 1:1 ether–hexane) gave 59 mg (77%) of **75**: mp 126–127 °C (ethyl acetate–hexane); ^1H NMR ($CDCl_3$, 90 MHz) δ 0.1–0.4 (br, 5 H, cyclopropyl), 0.65 (t, 3 H, CH_3, J = 7.1 Hz), 2.79 (d, 2 H, CH_2CO, J = 6.8 Hz), 3.71 (q, 2 H, OCH_2), 7.3–7.85 (m, 15 H, Ar); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 4.1 (C-6), 8.1 (C-5), 13.3 (CH_3), 45.3 (d, $^3J_{CP}$ = 6.7, C-4), 58.2 (OCH_2), 70.6 (d, $^1J_{CP}$ = 110.1 Hz, C-2), 127.2 (d, $^1J_{CP}$ = 94 Hz, Ph), 128.4 (d, $^2J_{CP}$ = 12.1 Hz, Ph), 131.4 (d, $^4J_{CP}$ = 4 Hz, Ph), 133.1 (d, $^3J_{CP}$ = 10.7 Hz, Ph), 167.8 (d, $^2J_{CP}$ = 16.2 Hz, C-1), 197.6 (d, $^2J_{CP}$ = 4 Hz, C-3). Anal. Calcd for $C_{27}H_{27}O_3P$: C, 75.33; H, 6.32. Found: C, 75.37; H, 6.57.

Ethyl 6-Chloro-2(*E*)-hexenoate (39). To a stirred suspension of NaH (0.055 mol, pentane washed) in 160 mL of THF was added over 5 min 10.3 mL (0.052 mol) of triethyl phosphonoacetate. After H_2 evolution was complete (5 min), a solution containing 5.3 g (0.05 mol) of 4-chlorobutanal (**37**)[40] in 10 mL of THF was

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added over 0.5 min. The mixture was stirred for 1.5 h and then concentrated in vacuo. The residue was treated with water and extracted with pentane. The organic phase was washed with water and concentrated on a steam bath to give a residual oil that, upon distillation, gave 6.6 g (75%) of **39**: bp 118–122 °C (13 mm); IR (neat) ν 1705, 1635 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ 1.28 (t, 3 H, OCH_2CH_3, J = 7.1 Hz), 1.7–2.1 (m, 2 H, CH_2), 2.2–2.6 (m, 2 H, allylic CH_2), 3.55 (t, 2 H, CH_2Cl, J = 6.4 Hz), 4.18 (q, 2 H, OCH_2), 5.87 (dt, C=CHCO, J = 15.6, 1.5 Hz), 6.93 (dt, CH=C-HCO, J = 15.6, 6.9 Hz). Anal. Calcd for $C_8H_{13}ClO_2$: C, 54.39; H, 7.36. Found: C, 54.01; H, 7.72.

Ethyl 8-Chloro-3-oxo-2-(triphenylphosphoranylidene)-4-(*E*)-octenoate (43). To a solution containing 1.2 g (18 mmol) of KOH in 4 mL of water were added 2.82 g (16 mmol) of chloro ester **39** and enough EtOH (8-10 mL) to give a homogeneous solution. After stirring for 6 h, the mixture was concentrated in vacuo, treated with 20 mL of brine, acidified with concentrated HCl, and extracted with 1:1 Et_2O–pentane. The extracts were washed with brine (2 × 15 mL) and dried over Na_2SO_4. Solvent removal followed by short-path distillation [bp 90–95 °C (0.1 mm)] gave 1.97 g (83%) of 6-chloro-2-hexenoic acid (**41**), which was used without further purification. Oxalyl chloride (3.4 mL, 40 mmol) in 15 mL of benzene was treated dropwise, with stirring, with 1.94 g (13 mmol) of acid **41** in 3 mL of benzene over 2 min. The solution was stirred at 40 °C under a slow stream of argon for 1 h and then concentrated in vacuo. The residual oil was reconcentrated four times from benzene solution, dissolved in 10 mL of fresh benzene, and added to a stirred 5 °C solution containing 9.0 g (26 mmol) of (carboethoxymethylene)triphenylphosphorane[44] in 90 mL of benzene. The mixture was stirred at 5 °C for 10 min and then allowed to come to 20 °C whereupon stirring was continued for 0.5 h. The mixture was treated with an equal volume of Et_2O and filtered to remove the phosphonium salt. Solvent removal followed by chromatography (silica gel, 10:1 CH_2Cl_2–EtOAc) gave 9.95 g (80%) of **43** as an oil that slowly solidified: mp 125–127 °C (from EtOAc–pentane); ^1H NMR ($CDCl_3$, 90 MHz) δ 0.65 (t, 3 H, OCH_2CH_3, J = 7.1 Hz), 1.7–2.1 (m, 2 H, CH_2), 2.1–2.5 (m, 2 H, CH_2), 3.54 (t, 2 H, J = 6.3 Hz), 3.72 (q, 2 H, OCH_2, J = 7.1 Hz), 6.58 (dt, 1 H, allylic, J = 16, 7 Hz), 7.3–8.0 (br, 16 H, Ph). Anal. Calcd for $C_{28}H_{28}ClPO_3$: C, 70.22; H, 5.89. Found: C, 70.40; H, 5.89.

Ethyl 8-Iodo-3-oxo-2-(triphenylphosphoranylidene)-4-(*E*)-octenoate (45). A mixture containing 1.44 g (3 mmol) of **43**, 4.5 g (30 mmol) NaI, and 25 mL of acetone was stirred at 55 °C for 25 h. The residue obtained after concentration in vacuo was treated with water and extracted with Et_2O. The extracts were washed sequentially with water (2×), 5% $NaHSO_3$, water, and brine, dried (Na_2SO_4), and concentrated, giving 1.54 g (90%) of **45** as a thick oil: ^1H NMR ($CDCl_3$, 60 MHz) δ 0.67 (t, 3 H, OCH_2CH_3, J = 7.5 Hz), 1.7–2.6 (m, 4 H, CH_2), 3.27 (t, 2 H, CH_2I, J = 7 Hz), 3.79 (q, 2 H, OCH_2), 6.77 (dt, 1 H, C-4 H, J = 16, 7 Hz), 7.5–8.3 (br, 16 H, Ph). Samples of this iodide were reconcentrated repeatedly from benzene solution and dried under vacuum prior to use.

Ethyl 8-Bromo-3-oxo-2-(triphenylphosphoranylidene)-4-(*E*)-octenoate (47). A solution containing 1.0 g (2.1 mmol) of **43**, 5 g (49 mmol) of NaBr, 2.5 mL of EtBr, and 5 mL of *N*-methylpyrrolidone was heated in a 60–70 °C bath with stirring for 3 days in a flask equipped with an efficient condenser.[42] Each day the condenser was removed briefly to allow most of the EtCl and EtBr to distill from the vessel followed by the addition of a fresh portion (2.5 mL) of EtBr and resumed heating. The cooled mixture was diluted with water and extracted with CH_2Cl_2. The extracts were washed repeatedly with water, dried over Na_2SO_4, and concentrated. PTLC (silica gel, 7:1 CH_2Cl_2–EtOAc) gave 760 mg (70%) of **47**, which by ^1H NMR analysis contained 7% of unreacted chloride **43**. Recrystallization from EtOAc–hexane gave pure **47**: mp 117–118 °C; ^1H NMR ($CDCl_3$, 90 MHz) δ 0.64 (t, 3 H, OCH_2CH_3, J = 7.1 Hz), 1.8–2.2 (m, 2 H, CH_2), 2.2–2.5 (m, 2 H, CH_2), 3.38 (t, 2 H, CH_2Br, J = 6.6 Hz), 3.72 (q, 2 H, OCH_2), 6.58 (dt, 1 H, allylic, J = 15.4, 6.4 Hz), 7.25–7.85 (m, 16 H, Ph and vinyl). Anal. Calcd for $C_{28}H_{28}BrO_3P$: C, 64.25; H, 5.39. Found: C, 64.40; H, 5.48.

Cyclization of 45 with *n*-BuLi. A solution containing 160 mg (0.28 mmol) of **45** in 3 mL of THF was cooled to −100 °C, and with stirring there was added over 6 min 0.30 mL (0.42 mmol) of cold (−78 °C) 1.4 M *n*-BuLi solution. After 4 min, 100 μL of MeOH was added and the mixture was warmed to 25 °C and evaporated to dryness under reduced pressure. The residue was purified by PTLC (8:1 CH_2Cl_2–EtOAc), giving 100 mg (80%) of ethyl 4-cyclobutyl-3-oxo-2-(triphenylphosphoranylidene)butanoate (**76**): mp 137–139 °C (EtOAc–hexane); ^1H NMR ($CDCl_3$, 90 MHz) δ 0.65 (t, 3 H, OCH_2CH_3, J = 7.1 Hz), 1.5–2.2 (br, 6 H, cyclobutyl CH_2), 2.5–3.1 (m, 3 H, CH_2CO and CH), 3.72 (q, 2 H, CH_2O, J = 7.1 Hz), 7.2–7.8 (m, 15 H, Ar); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 13.8 (OCC), 18.8 (C-3′), 28.5 (C-2′), 33.4 (C-1′), 47.2 (d, C-4, $^1J_{CP}$ = 5.4 Hz), 58.2 (OC), 71.0 (d, C-2, J = 110.1 Hz), 127.2 (d, Ph, $^1J_{CP}$ = 94.0 Hz), 128.3 (d, Ph, $^2J_{CP}$ = 12.1 Hz), 131.3 (d, Ph, $^4J_{CP}$ = 2.7 Hz), 133.0 (d, Ph, $^3J_{CP}$ = 10.8 Hz), 167.8 (d, C-1, $^2J_{CP}$ = 14.8 Hz), 197.1 (d, C-3, $^2J_{CP}$ = 2.7 Hz). Anal. Calcd for $C_{28}H_{29}O_3P$: C, 75.66; H, 6.58. Found: C, 75.59; H, 6.75.

Cyclization of 45 with *t*-BuLi. To a solution containing 188 mg (0.33 mmol) of **45** in 3 mL of THF at −100 °C was added 0.68 mL (0.75 mmol) of cold (−78 °C) 1.11 M *t*-BuLi over 5 min. The bath was allowed to warm to −68 °C over 12 min whereupon 100 μL (1.6 mmol) of MeI was added. The mixture was allowed to warm to 25 °C over 5 min and was stirred at 40 °C for 10 min. The solvent was removed under reduced pressure and chromatography of the residue (PTLC, 9:1 CH_2Cl_2–EtOAc) gave 110 mg (73%) of **77**: mp 154.5–156.5 °C (EtOAc–hexane); ^1H NMR ($CDCl_3$, 90 MHz) δ 0.64 (t, 3 H, OCH_2CH_3, J = 7.1 Hz), 1.00 (d, 3 H, CH_3, J = 6.8 Hz), 1.5–2.2 (br, 6 H, cyclobutyl CH_2), 2.2–2.8 (br, 1 H, cyclobutyl CH), 3.71 (q, 2 H, OCH_2, J = 7.1 Hz), 3.4–4.1 (m, 1 H, C-4H), 7.2–7.8 (m, 15 H, Ph); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 13.7 (OCC), 15.0 (CH_3), 18.2 (C-3′), 26.8 (C-2′), 27.0 (C-4′), 39.3 (C-1′), 46.5 (d, C-4, $^3J_{CP}$ = 6.7 Hz), 58.2 (OC), 71.5 (d, C-2, $^1J_{CP}$ = 108.8 Hz), 127.4 (d, Ph, $^1J_{CP}$ = 92.7 Hz), 128.3 (d, Ph, $^2J_{CP}$ = 12.1 Hz), 131.2 (d, Ph, $^4J_{CP}$ = 4.0 Hz), 132.9 (d, Ph, $^3J_{CP}$ = 10.7 Hz), 167.5 (d, C-1, $^2J_{CP}$ = 14.8 Hz), 200.4 (d, C-3, $^2J_{CP}$ = 2.7 Hz). Anal. Calcd for $C_{29}H_{31}O_3P$: C, 75.96; H, 6.82. Found: C, 75.73; H, 6.78.

Reaction of 47 with *n*-BuLi. To a solution containing 160 mg (0.3 mmol) of **47** in 3 mL of THF at −100 °C was added, with stirring, over 4 min, 0.25 mL (0.35 mmol) of cold (−78 °C) 1.4 M *n*-BuLi. After 8 min the mixture was slowly warmed to 40 °C and stirred for 30 min. Solvent was removed under reduced pressure, and chromatography of the residue (PTLC, 10:1 CH_2Cl_2–EtOAc) gave 130 mg (87%) of **82** as an oil: ^1H NMR ($CDCl_3$, 90 MHz) δ 0.65 (t, 3 H, OCH_2CH_3, J = 7.1 Hz), 0.84 (t, 3 H, CH_3), 1.0–1.4 (br, 8 H, CH_2), 1.4–1.9 (br, 4 H, CH_2), 1.9–2.3 (m, 1 H, ring CH), 3.71 (t, 2 H, OCH_2, J = 7.1 Hz), 3.5–3.9 (br, 1 H, CHCO), 7.2–7.8 (m, 15 H, Ar); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 13.7 (OCC), 14.1, 22.9, 24.8, 30.8, 31.6, 32.8, 35.0, 42.9 (BuC), 52.9 (d, CCO $^3J_{CP}$ = 5.4 Hz), 58.2 (OC), 71.7 (d, C-2, $^1J_{CP}$ = 110.1 Hz), 127.5 (d, Ph, $^1J_{CP}$ = 94.0 Hz), 128.3 (d, Ph, $^2J_{CP}$ = 12.0 Hz), 131.2 (d, Ph, $^4J_{CP}$ = 2.7 Hz), 132.9 (d, Ph, $^3J_{CP}$ = 9.4 Hz), 167.5 (d, C-1, $^2J_{CP}$ = 14.8 Hz), 200.1 (d, C-3, $^2J_{CP}$ = 2.7 Hz).

Ethyl 7-Chloro-2(*E*)-heptenoate (40). By the procedure described for the preparation of **39**, 12.0 g (0.1 mol) of 5-chloropentanal[43] gave 14.5 g (76%) of **40**: bp 129–131 °C (13 mm); ^1H NMR (CCl_4, 60 MHz) δ 1.28 (t, 3 H, OCH_2CH_3, J = 7 Hz), 1.7–2.2 (m, 2 H, C-5 H), 2.2–2.7 (m, 2 H, allylic H), 3.60 (t, 2 H, CH_2Cl, J = 6.5 Hz), 4.20 (q, 2 H, OCH_2, J = 7 Hz), 5.93 (dt, 1 H, C-2 H, J = 16, 2 Hz), 7.03 (dt, 1 H, C-3 H, J = 16, 7 Hz). Anal. Calcd for $C_9H_{15}ClO_2$: C, 56.69; H, 7.93. Found: C, 56.43; H, 8.14.

7-Chloro-2(*E*)-heptenoic Acid (42). To a solution containing 3.5 g (53 mmol) of KOH in 10 mL of water was added 9.5 g of **40**. Ethanol (20–25 mL) was added with stirring until the solution became homogeneous, and stirring was continued overnight. The mixture was concentrated under reduced pressure, treated with 10 mL of water, and extracted with ether to remove neutral materials. The aqueous layer was saturated with NaCl, acidified with concentrated HCl, and extracted with ether. The extracts were washed twice with brine, dried over Na_2SO_4, and concen-

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trated on a steam bath. Distillation gave 6.8 g (84%) of **42** as an oil: bp 118–121 °C (0.15 mm); ^{1}H NMR (CCl_4, 60 MHz) δ 1.65–2.25 (m, 2 H, CH_2), 2.25–2.70 (m, 2 H, allylic CH_2), 3.60 (t, 2 H, CH_2Cl, J = 6.5 Hz), 5.97 (dt, 1 H, C-2 H, J = 16, 2 Hz), 7.17 (dt, 1 H, C-3 H, J = 16, 7 Hz), 12.0 (s, 1 H, COOH). Anal. Calcd for $C_7H_{11}ClO_2$: C, 51.70; H, 6.82. Found: C, 51.55; H, 6.83.

Ethyl 9-Chloro-3-oxo-2-(triphenylphosphoranylidene)-4-(*E*)-nonenoate (44). By the procedure described above for the preparation of **43**, 4.9 g (30 mmol) of **42** was converted to its acid chloride, which was treated with 21 g (60 mmol) of ethyl (triphenylphosphoranylidene)acetate to give, after chromatography (silica, 10:1 CH_2Cl_2–EtOAc), 12.8 g (87%) of **44** as a thick oil: ^{1}H NMR ($CDCl_3$, 60 MHz) δ 0.67 (t, 3 H, OCH_2CH_3, J = 7 Hz), 1.5–2.0 (br, 4 H, CH_2), 2.0–2.5 (m, 2 H, allylic CH_2), 3.60 (t, 2 H, CH_2Cl, J = 6.5 Hz), 3.83 (q, 2 H, OCH_2, J = 7 Hz), 6.78 (dt, 1 H, C-4 H, J = 15.5, 7 Hz), 7.3–8.1 (br, 16 H, Ph and C-5 H); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 13.7 (OCC), 25.8, 31.4, 32.1, 44.8, 58.5 (OC), 71.6 (d, C-2, $^1J_{CP}$ = 111.5 Hz), 127.0 (d, Ph, $^1J_{CP}$ = 94.0 Hz), 128.5 (d, Ph, $^2J_{CP}$ = 12.1 Hz), 129.4 (C-4), 131.5 (d, Ph, $^4J_{CP}$ = 2.7 Hz), 132.5 (d, Ph, $^3J_{CP}$ = 9.4 Hz), 140.1 (C-5), 167.7 (d, C-1, $^2J_{CP}$ = 14.8 Hz), 186.6 (d, C-3, $^2J_{CP}$ = 4.0 Hz).

Ethyl 9-Iodo-3-oxo-2-(triphenylphosphoranylidene)-4-(*E*)-nonenoate (46). In the manner described for the preparation of **45**, 1.5 g (3 mmol) of **44** gave 1.55 g (87%) of **46** as a thick oil: ^{1}H NMR ($CDCl_3$, 60 MHz) δ 0.67 (t, 3 H, OCH_2CH_3, J = 7 Hz), 1.3–2.0 (m, 4 H, CH_2), 2.0–2.5 (m, 2 H, allylic CH_2), 3.23 (t, 2 H, CH_2I), 3.83 (t, 2 H, OCH_2, J = 7 Hz), 6.75 (dt, 1 H, C-4 H, J = 16, 7 Hz), 7.2–8.1 (m, 16 H, Ph and C-5 H). Samples of this iodide were reconcentrated repeatedly from benzene solution and dried under vacuum prior to use.

Cyclization of 46 with *n*-BuLi. A solution containing 150 mg (0.26 mmol) of **46** in 3 mL of THF was cooled to −100 °C, and with stirring there was added over 4 min 0.25 mL (0.35 mmol) of 1.4 M *n*-BuLi. The mixture was stirred for 2 min whereupon 100 μL of MeOH was added, and the solvent was removed under reduced pressure. Chromatography (PTLC, 8:1 CH_2Cl_2–EtOAc) gave 90 mg (77%) of **78**: mp 116–118 °C (EtOAc–pentane); ^{1}H NMR ($CDCl_3$, 100 MHz) δ 0.66 (t, 3 H, OCH_2CH_3, J = 7 Hz), 1.0–2.0 (br, 8 H, ring CH_2), 2.1–2.6 (m, 1 H, CH), 2.96 (d, 2 H, CH_2CO, J = 7 Hz), 3.76 (q, 2 H, OCH_2, J = 7 Hz), 7.3–7.9 (m, 15 H, Ph). Anal. Calcd for $C_{29}H_{31}PO_3$: C, 75.96; H, 6.81. Found: C, 75.85; H, 6.71.

Ethyl 10-Chloro-3-oxo-2-(triphenylphosphoranylidene)-4(*E*)-decenoate (49). To a stirred suspension of 240 mg (5.7 mmol) of 57% NaH–oil dispersion in 25 mL of THF were added 3.03 g (5.8 mmol) of **15** and 673 mg (5.13 mmol) of 6-chlorohexanal (**48**).[44] After approximately 5 min, vigorous H_2 evolution began, and stirring was continued for 0.5 h. The solvent was removed under reduced pressure, 15 mL of water was added, and the mixture was extracted with CH_2Cl_2. The organic phase was washed twice with water, dried (Na_2SO_4), and concentrated. Chromatography (10:1 CH_2Cl_2–EtOAc) gave 2.28 g (88%) of **49** as a thick oil: ^{1}H NMR ($CDCl_3$, 90 MHz) δ 0.64 (t, 3 H, OCH_2CH_3, J = 7.1 Hz), 1.2–1.9 (br, 6 H, CH_2), 2.0–2.3 (m, 2 H, allylic CH_2), 3.47 (t, 2 H, CH_2Cl, J = 6.6 Hz), 3.72 (q, 2 H, OCH_2, J = 7.1 Hz), 6.62 (dt, 1 H, C-4 H, J = 15.4, 6.8 Hz), 7.3–7.8 (m, 15 H, Ph); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 13.6 (OCC), 26.5, 27.7, 32.0, 32.4, 44.8 (CCl), 58.3 (OC), 71.5 (d, C-2, $^1J_{CP}$ = 111.5 Hz), 127.0 (d, Ph, $^1J_{CP}$ = 94.0 Hz), 128.4 (d, Ph, $^2J_{CP}$ = 12.1 Hz), 131.4 (d, Ph, $^4J_{CP}$ = 2.7 Hz), 132.9 (d, Ph, $^3J_{CP}$ = 9.4 Hz), 140.5 (C-5), 167.6 (d, C-1, $^2J_{CP}$ = 14.8 Hz), 186.6 (d, C-3, $^2J_{CP}$ = 4.0 Hz).

Ethyl 10-Iodo-3-oxo-2-(triphenylphosphoranylidene)-4-(*E*)-decenoate (50). This iodide was prepared in 87% yield by the procedure described for the preparation of **45** and was a thick oil: ^{1}H NMR ($CDCl_3$, 90 MHz) δ 0.65 (t, 3 H, OCH_2CH_3, J = 7.1 Hz), 1.1–1.6 (br, 4 H, CH_2), 1.6–2.0 (m, 2 H, CH_2, 2.0–2.35 (m, 2 H, allylic CH_2), 3.16 (t, 2 H, CH_2I, J = 7.1 Hz), 3.72 (q, 2 H, OCH_2, J = 7.1 Hz), 6.61 (dt, 1 H, C-4 H, J = 15.4, 6.8 Hz), 7.2–7.9 (m, 16 H, Ph and C-5 H); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 6.8 (CH_2I), 13.7 (OCC), 27.5, 30.2, 32.1, 33.4, 58.4 (OC), 71.5 (d, C-2, $^1J_{CP}$ = 111.5 Hz), 127.0 (d, Ph, $^1J_{CP}$ = 94.0 Hz) 128.5 (d, Ph, $^2J_{CP}$ = 12.1 Hz), 131.4 (d, Ph, $^4J_{CP}$ = 4.0 Hz), 133.0 (d, Ph, $^3J_{CP}$ = 9.4 Hz), 140.7 (C-5), 167.7 (d, C-1, $^2J_{CP}$ = 14.8 Hz), 186.7 (d, C-3, $^2J_{CP}$ = 4.0 Hz).

Cyclization of 50 with *n*-BuLi. To a solution containing 170 mg (0.28 mmol) of **50** in 3 mL of THF at −100 °C was added with vigorous stirring over 4 min 0.28 mL (0.39 mmol) of cold (−78 °C) 1.4 M *n*-BuLi. After 7 min, 100 μL of MeOH was added, the mixture was warmed to 25 °C, and the solvent was removed under reduced pressure. Chromatography of the residue (PTLC, 10:1 CH_2Cl_2–EtOAc) gave 60 mg (44%) of **79**: mp 136–138 °C (EtOAc–hexane); ^{1}H NMR ($CDCl_3$, 60 MHz) δ 0.67 (t, 3 H, OCH_2CH_3, J = 7 Hz), 1.0–1.9 (br, 10 H, CH_2), 1.9–2.3 (br, 1 H, CH), 2.83 (d, 2 H, CH_2CO, J = 7.5 Hz), 3.80 (q, 2 H, OCH_2, J = 7 Hz), 7.2–8.1 (br, 15 H, Ph). Anal. Calcd for $C_{30}H_{33}O_3P$: C, 76.25; H, 7.04. Found: C, 76.26; H, 6.86.

Ethyl 6-Chloro-3-methyl-2-hexenoate (52). NaH (1.73 g, 38 mmol, 50% in oil) was freed of oil by washing with pentane and then suspended in 100 mL of THF. With stirring, 8.1 g (36 mmol) of triethyl phosphonoacetate was added over several minutes, and stirring was continued until H_2 evolution was complete. 5-Chloro-2-pentanone[46] (4.2 g, 35 mmol) was added in one portion, and the mixture was stirred for 1 h. THF was removed under reduced pressure, and the residue was treated with 50 mL of water. The mixture was extracted with pentane, and the extracts were dried (Na_2SO_4) and concentrated. Distillation gave 3.31 g (50%) of **52** as a mixture of isomers: bp 127–130 °C (12 mm). Nearly pure (*E*)-**52** could be obtained by chromatography on silica (CH_2Cl_2): ^{1}H NMR ($CDCl_3$, 90 MHz) δ 1.30 (t, 3 H, OCH_2CH_3, J = 7.1 Hz), 1.5–2.4 (m, 4 H, CH_2), 2.20 (d, 3 H, CH_3, J = 1.3 Hz), 3.57 (t, 2 H, CH_2Cl, J = 6.5 Hz), 4.18 (q, 2 H, OCH_2, J = 7.1 Hz), 5.75 (m, 1 H, olefinic). Anal. Calcd. for $C_9H_{15}ClO_2$: C, 56.69; H, 7.93. Found: C, 56.53; H, 8.04.

6-Chloro-3-methyl-2-hexenoic Acid (53). To a solution containing 3.3 g (17 mmol) of **52** and 1.2 g (18 mmol) of KOH in 5 mL of water was added EtOH until the mixture became homogeneous. The solution was stirred overnight and then concentrated under reduced pressure. Water (20 mL) was added, and neutral materials were removed by ether extraction. The aqueous phase was saturated with NaCl, acidified with concentrated HCl, and extracted with ether. The dried extracts (Na_2SO_4) were concentrated, and the residue gave, upon bulb-to-bulb distillation (130 °C, 0.1 mm), 1.17 g (42%) of **53** as an oil: ^{1}H NMR (*E* isomer, $CDCl_3$, 90 MHz) δ 1.3–2.9 (m, 4 H, CH_2), 2.18 (d, 3 H, CH_3, J = 1.2 Hz), 3.54 (t, 2 H, CH_2Cl, J = 5.1 Hz), 5.73 (br s, 1 H, olefinic), 11.04 (br s, 1 H, OH). Anal. Calcd for $C_7H_{11}ClO_2$: C, 51.70; H, 6.82. Found: C, 51.63; H, 6.90.

Ethyl 8-Chloro-5-methyl-3-oxo-2-(triphenylphosphoranylidene)-4(*E*,*Z*)-octenoate (54). To a solution containing 2.8 g (22 mmol) of $(COCl)_2$ in 8.3 mL of benzene was added over several minutes 1.17 g (7.2 mmol) of **53**. The mixture was stirred at 40 °C for 1 h and then under reflux for 20 min. Volatiles were then removed under reduced pressure [30–45 °C (30 mm)], and the residue was reconcentrated four times from benzene solution and dissolved in 5 mL of benzene. This solution was added with stirring to a cold (8 °C) solution containing 4.97 g (14.3 mmol) of ethyl (triphenylphosphoranylidene)acetate in 50 mL of benzene, and stirring was continued at 8 °C for 10 min and 30 min at 25 °C. Ether (25 mL) was added, and the phosphonium salt was removed by filtration. The filtrate was washed with water, dried over Na_2SO_4, and evaporated under reduced pressure. Chromatography (PTLC, 7:1 CH_2Cl_2–EtOAc) gave 1.52 g (43%) of (*E* and *Z*)-**54** as an oil: ^{1}H NMR (*E* isomer, $CDCl_3$, 90 MHz) δ 0.63 (t, 3 H, OCH_2CH_3, J = 7.1 Hz), 1.5–2.3 (m, 4 H, CH_2), 1.89 (d, 3 H, CH_3, J = 1.2 Hz), 3.56 (t, 2 H, CH_2Cl, J = 6.3 Hz).

Ethyl 8-Iodo-5-methyl-3-oxo-2-(triphenylphosphoranylidene)-4(*E*)-octenoate (55). In the manner previously described for the preparation of **58**, 175 mg of **54** gave, after PTLC (7:1 CH_2Cl_2–EtOAc), 105 mg (51%) of **55** as an oil. The *E* isomer could be obtained from the lower half of the chromatographic band: ^{1}H NMR ($CDCl_3$, 90 MHz) δ 0.64 (t, 3 H, OCH_2CH_3, J = 7.1 Hz), 1.7–2.3 (m, 4 H, CH_2), 1.87 (d, 2 H, CH_3, J = 1.2 Hz), 3.21 (t, 2 H, CH_2I, J = 6.6 Hz), 3.71 (q, 2 H, OCH_2, J = 7.1 Hz), 7.02 (br s, 1 H, olefinic), 7.2–7.9 (m, 15 H, Ph); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 6.6 (C-8), 13.8 (OCC), 18.9 (5-Me), 31.5 (C-7), 41.1 (C-6), 58.2 (OC), 72.5 (d, C-2, $^1J_{CP}$ = 111.5 Hz), 126.1 (d, C-4, $^3J_{CP}$ = 8.1 Hz), 127.1 (d, Ph, $^1J_{CP}$ = 94.0 Hz), 128.4 (d, Ph, $^2J_{CP}$ = 12.1 Hz), 131.4 (d, Ph, $^4J_{CP}$ = 2.7 Hz), 133.0

(46) Cannon, G. W.; Ellis, R. C.; Leal, J. R. *Organic Syntheses*; Wiley: New York, 1963; Collect. Vol. IV, p 597.

(d, Ph, $^3J_{CP}$ = 9.4 Hz), 145.5 (C-6), 167.5 (d, C-1, $^2J_{CP}$ = 14.8 Hz), 189.3 (d, C-3, $^2J_{CP}$ = 2.0 Hz). This iodide was twice concentrated from benzene solution and dried under vacuum prior to use.

Reaction of 55 with *n*-BuLi. A solution containing 170 mg (0.29 mmol) of (*E*)-**55** in 5 mL of THF was cooled to −78 °C, and with vigorous stirring there was added over 15 min a −78 °C solution (0.25 mL, 0.34 mmol) of 1.36 M *n*-BuLi. After 3 min, 100 μL of EtOH was added, and after warming to 25 °C, the solvent was removed under reduced pressure. The residue was dissolved in CH_2Cl_2 and washed with water. Concentration of the dried extract (Na_2SO_4) and PTLC (7:1 CH_2Cl_2–EtOAc) gave 100 mg (75%) of **80**: mp 133–135 °C (EtOAc–hexane); ^{1}H NMR ($CDCl_3$, 90 MHz) δ 0.66 (t, 3 H, OCH_2CH_3, *J* = 7.1 Hz), 1.15 (s, 3 H, CH_3), 1.4–2.2 (m, 6 H, CH_2), 3.03 (s, 2 H, CH_2CO), 3.70 (q, 2 H, OCH_2, *J* = 7.1 Hz), 7.2–7.9 (m, 15 H, Ph); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 13.8 (OCC), 15.6 (Me), 27.1 (C-3′), 33.8 (C-2′, C-4′), 38.6 (C-1′), 49.9 (d, C-4, $^3J_{CP}$ = 5.4 Hz), 58.2 (OC), 72.8 (d, C-2, $^1J_{CP}$ = 110.1 Hz), 127.3 (d, Ph, $^1J_{CP}$ = 94.0), 128.3 (d, Ph, $^2J_{CP}$ = 12.1 Hz), 131.3 (d, Ph, $^4J_{CP}$ = 2.7 Hz), 131.1 (d, Ph, $^4J_{CP}$ = 10.7 Hz), 167.9 (d, C-1, $^2J_{CP}$ = 14.8 Hz), 196.6 (d, C-3, $^2J_{CP}$ = 4.0 Hz). Anal. Calcd for $C_{29}H_{31}O_3P$: C, 75.96; H, 6.81. Found: C, 75.92; H, 6.90.

Ethyl 9-Chloro-5-methyl-3-oxo-2-(triphenylphosphoranylidene)-4-nonenoate (57). In a 50-mL flask was placed 42 mg (1.0 mmol) of 50% NaH, which was freed of oil by washing with two portions of pentane and then suspended in 10 mL of THF. There was added 529 mg (1.0 mmol) of **15** and two drops of *i*-PrOH. Stirring was continued until H_2 evolution ceased (15 min) whereupon 135 mg (1.0 mmol) of 6-chloro-2-hexanone[45] was added and stirring was continued overnight. The solvent was removed under reduced pressure and chromatography of the residue (PTLC, 5:1 CH_2Cl_2–EtOAc) gave 250 mg (50%) of **57** as a thick oil as a mixture (~3:1) of *E* and *Z* isomers. The major *E* isomer was obtained from the top of the PTLC product zone: ^{1}H NMR ($CDCl_3$, 90 MHz) δ 0.63 (t, 3 H, OCH_2CH_3, *J* = 7.1 Hz), 1.3–2.3 (br, 6 H, CH_2), 1.88 (br s, 3 H, CH_3), 3.51 (t, 2 H, CH_2Cl, *J* = 6.6 Hz), 3.71 (q, 2 H, OCH_2, *J* = 7.1 Hz), 7.07 (br s, 1 H, olefinic), 7.2–7.9 (m, 15 H, Ph). The *Z* isomer has resonances at δ 1.82 (br s, CH_3) and 3.33 (t, CH_2Cl).

Ethyl 9-Iodo-5-methyl-3-oxo-2-(triphenylphosphoranylidene)-4(*E*)-nonenoate (58). A solution containing 253 mg (0.5 mmol) of (*E*)-**57** and 1.2 g of NaI in 1 mL of acetone was heated in a 65 °C bath for 12 h. The cooled mixture was poured into water and extracted with CH_2Cl_2. The residue obtained after solvent removal gave upon PTLC (5:1 CH_2Cl_2–EtOAc) 150 mg (50%) of **58** as a thick oil: ^{1}H NMR ($CDCl_3$, 90 MHz) δ 0.64 (t, 3 H, OCH_2CH_3, *J* = 7.1 Hz), 1.2–2.0 (br, 4 H, CH_2), 1.87 (d, 3 H, CH_3, *J* = 1.2 Hz), 2.13 (m, 2 H, allylic CH_2), 3.19 (t, 2 H, CH_2I, *J* = 6.6 Hz), 3.71 (q, 2 H, OCH_2, *J* = 7.1 Hz), 7.03 (br s, 1 H, olefinic), 7.2–7.9 (m, 15 H, Ph); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 6.9 (CH_2I), 13.8 (OCC), 18.7 (CH_3), 28.3 (C-6), 33.1, 39.4, 58.2 (OC), 72.4 (d, C-2, $^1J_{CP}$ = 112.8 Hz), 125.5 (d, C-4, $^3J_{CP}$ = 9.4 Hz), 127.2 (d, Ph, $^1J_{CP}$ = 94.0 Hz), 128.3 (d, Ph, $^2J_{CP}$ = 12.1 Hz), 131.3 (d, Ph, $^4J_{CP}$ = 2.7 Hz), 133.0 (d, Ph, $^3J_{CP}$ = 9.4 Hz), 147.1 (C-5) 167.5 (d, C-1, $^2J_{CP}$ = 14.8 Hz), 189.4 (d, C-3, $^2J_{CP}$ = 4.0 Hz). This iodide was found to decompose over the course of several days and was used immediately after twice reconcentrating benzene solutions in vacuo and vacuum drying the residue.

Cyclization of 58 with *n*-BuLi. A stirred solution of iodide **58** (140 mg, 0.23 mmol) in 4 mL of THF was cooled to −100 °C, and 0.22 mL (0.3 mmol) of cold (−78 °C) 1.36 M *n*-BuLi was added over 2 min. After stirring for 8 min, 100 μL of EtOH was added whereupon the mixture was warmed to 20 °C and concentrated in vacuo. The residue was dissolved in CH_2Cl_2 and washed with water, and the dried extract (Na_2SO_4) was concentrated. Chromatography (PTLC, 6:1 CH_2Cl_2–EtOAc) gave 82 mg (76%) of **81**: mp 137.0–139.5 °C (EtOAc–hexane); ^{1}H NMR ($CDCl_3$, 90 MHz) δ 0.65 (t, 3 H, OCH_2CH_3, *J* = 7.1 Hz), 0.98 (s, 3 H, CH_3), 1.2–1.7 (br, 8 H, CH_2), 2.95 (s, 2 H, CH_2CO), 3.69 (q, 2 H, OCH_2, *J* = 7.1 Hz), 7.2–7.9 (m, 15 H, Ph); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 13.8 (OCC), 24.3 (C-3′), 26.6 (CH_3), 39.7 (C-2′), 42.5 (C-1′), 49.0 (d, C-4, $^3J_{CP}$ = 6.7 Hz), 58.3 (OC), 73.3 (d, C-2, $^1J_{CP}$ = 109 Hz), 127.4 (d, Ph, $^1J_{CP}$ = 92.7 Hz), 128.3 (d, Ph, $^2J_{CP}$ = 13.4 Hz), 131.3 (d, Ph, $^4J_{CP}$ = 2.7 Hz), 133.0 (d, Ph, $^3J_{CP}$ = 9.4 Hz), 167.9 (d, C-1, $^2J_{CP}$ = 16.1 Hz), 197.0 (d, C-3, $^2J_{CP}$ = 2.7 Hz). Anal. Calcd for $C_{30}H_{33}O_3P$: C, 76.25; H, 7.04. Found: C, 76.08; H, 7.20.

Ethyl 8-Bromo-3-oxo-2-(triphenylphosphoranylidene)-4-(*E*)-nonenoate (59). In the manner described for the preparation of **54**, 750 mg of 4-bromopentanal[24] gave 300 mg (12%) of **59** after chromatography (PTLC, 10:1 CH_2Cl_2–EtOAc) as an oil: ^{1}H NMR ($CDCl_3$, 90 MHz) δ 0.65 (t, 3 H, OCH_2CH_3, *J* = 7.1 Hz), 1.67 (d, 3 H, CH_3CH, *J* = 6.6 Hz), 1.7–2.1 (m, 2 H, CH_2), 2.1–2.5 (m, 2 H, allylic CH_2), 3.72 (q, 2 H, OCH_2, *J* = 7.1 Hz), 4.12 (m, 1 H, CHBr), 6.59 (dt, 1 H, C-4 H, *J* = 15.6, 6.1 Hz), 7.2–8.0 (m, 15 H, Ph).

Ethyl 8-Iodo-3-oxo-2-(triphenylphosphoranylidene)-4-(*E*)-nonenoate (60). A mixture of 200 mg (0.37 mmol) of **59**, 3 g of NaI, and 5 mL of acetone was heated under reflux for 36 h. Solvent was removed under reduced pressure, and the residue was treated with water and extracted with CH_2Cl_2. Concentration of the dried extracts (Na_2SO_4) followed by PTLC (5:1 CH_2Cl_2–EtOAc) gave 135 mg (63%) of **60** as a thick oil: ^{1}H NMR ($CDCl_3$, 90 MHz) δ 0.65 (t, 3 H, OCH_2CH_3, *J* = 7.1 Hz), 1.88 (d, 3 H, CH_3, *J* = 6.8 Hz), 1.5–2.5 (m, 4 H, CH_2), 3.72 (q, 2 H, OCH_2, *J* = 7.1 Hz), 4.15 (m, 1 H, CHI), 6.58 (dt, 1 H, C-4 H, *J* = 15.1, 6.4 Hz), 7.2–7.9 (m, 15 H, Ph); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 13.7 (OCC), 28.8, 29.5, 32.2, 41.5, 58.4 (OC), 71.7 (d, C-2, $^1J_{CP}$ = 111.5 Hz), 126.8 (d, Ph, $^1J_{CP}$ = 94.0 Hz), 128.5 (d, Ph, $^2J_{CP}$ = 12.1 Hz), 129.6 (d, C-4, $^3J_{CP}$ = 8.1 Hz), 131.5 (d, Ph, $^4J_{CP}$ = 2.7 Hz), 133.0 (d, Ph, $^3J_{CP}$ = 9.4 Hz), 138.7 (C-5), 167.6 (d, C-1, $^2J_{CP}$ = 14.8 Hz), 186.3 (d, C-3, $^2J_{CP}$ = 4.0 Hz). This iodide was reconcentrated twice from benzene solution and dried under vacuum prior to use.

Reaction of 60 with *n*-BuLi. A solution containing 130 mg (0.22 mmol) of **60** in 3 mL of THF was stirred at −78 °C and treated with 0.2 mL (0.28 mmol) of −78 °C 1.4 M *n*-BuLi solution over 2 min. After 15 min at −78 °C, the mixture was stirred at 20 °C for 15 min and then quenched with 100 μL of MeOH. The residue obtained after concentration was treated with water and extracted with CH_2Cl_2. Concentration of the dried extracts gave a complex mixture that was partially resolved by PTLC (10:1 CH_2Cl_2–EtOAc). The major product [R_f 0.60; 30 mg (27%)] is thought to be a diastereomer of **83** on the basis of the following NMR data: ^{1}H NMR ($CDCl_3$, 90 MHz) δ 0.67 (t, 3 H, OCH_2CH_3), 0.74 (d, 3 H, ring Me, *J* = 7.1 Hz), 0.84 (t, 3 H, butyl Me), 1.0–1.4 (br, 8 H, CH_2), 1.5–1.9 (br, 2 H, CH_2), 2.0–2.7 (m, 2 H, CH), 3.60–3.85 (m, 1 H, CHCO), 3.73 (q, 2 H, OCH_2, *J* = 7.1 Hz), 7.2–7.9 (m, 15 H, Ph); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ 13.8 (OCC), 14.1 (CH_3), 17.5, 23.1, 30.8, 31.5, 34.7, 35.6, 36.9, 41.2, 56.5 (d, CCO, $^3J_{CP}$ = 6.7 Hz), 58.2 (OC), 73.5 (d, C-2, $^1J_{CP}$ = 108.8 Hz), 127.6 (d, Ph, $^1J_{CP}$ = 92.7 Hz), 128.3 (d, Ph, $^2J_{CP}$ = 12.1 Hz), 131.3 (d, Ph, $^4J_{CP}$ = 4.0 Hz), 133.2 (d, Ph, $^3J_{CP}$ = 9.4 Hz), 167.8 (d, C-1, $^2J_{CP}$ = 16.1 Hz), 198.9 (d, C-3, $^2J_{CP}$ = 2.7 Hz). A second partially purified product [R_f 0.50; 23 mg (21%)] gave a similar ^{1}H NMR spectrum but with a methyl doublet at δ 1.07 (*J* = 6.4 Hz) and appears to be an isomer of **83**. Small amounts (9 mg) of a third impure product (R_f 0.44) were also isolated. Olefinic peaks near δ 5.0 and 5.35 ppm, a doublet at δ 2.82 (CH_2CO), and butyl peaks suggest structure **84**.

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