Formation and Alkylation of Lithium Enolates from Enol Phosphorylated Species[1]

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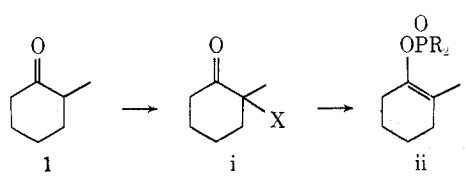
The cleavage of vinyl phosphinates, vinyl phosphonates, or vinyl phosphates, derived from cyclic α-halo ketones, with methyl- or butyllithium smoothly yields the corresponding lithium enolate and inert phosphorus-containing by-products. Cleavage of enol triphenylphosphonium halides occurs but is complicated by the formation of biphenyl and triphenylphosphine as by-products and by the hydrolytic instability of the starting compounds. The lithium enolates thus formed can be regiospecifically monoalkylated on carbon in good yield. Polyalkylation occurs as a minor process mainly in methylation and is negligible for larger alkyl groups. Alkylation of several enolates, formed from ketones with lithium triphenylmethide, gives comparable results. A notable exception to the regiospecificity of the alkylations occurs with the less substituted lithium enolate of 2-methylcyclohexanone, which gives 2-methyl-2-butylcyclohexanone and not the desired 2-methyl-6-butylcyclohexanone. Corresponding methylation gives 2,6-dimethylcyclohexanone. The cleavage and alkylation of derivatives of acetone and butyraldehyde are described. The preparation of 2-methyl-6-bromocyclohexanone is discussed.

The conversion of α-halo ketones to vinyl phosphates occurs smoothly in high yield.[3,4] Vinyl phosphinates and phosphonates are also available from the reactions of α-halo ketones with alkyl diphenylphosphinites and dialkyl phenylphosphonites.[5] Less generally, some halo ketones can be converted to enol triphenylphosphonium salts upon reaction with triphenylphosphine (TPP).[6] This procedure avoids obtaining mixtures of the two possible enol derivatives of an unsymmetrical ketone as sometimes found in the formation of enol acetates[7] or enol trimethylsilyl ethers.[8,9]

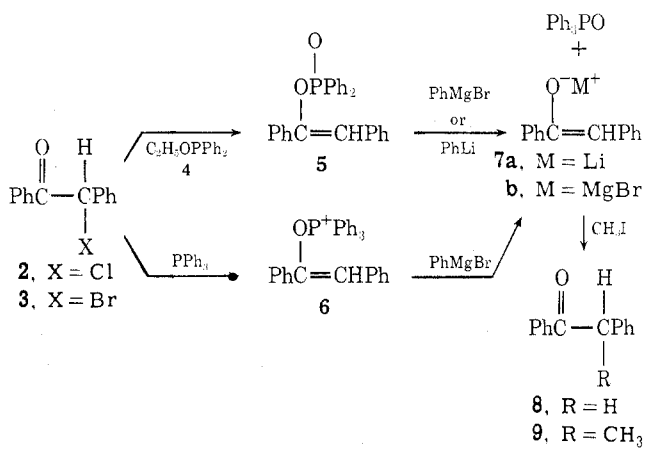


1 i ii

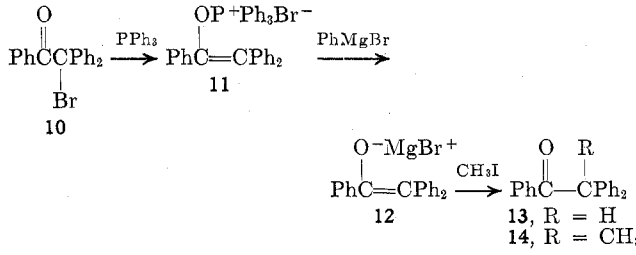
It was felt that enol phosphorylated species should be cleaved by strong bases to give lithium or magnesium enolates, which could then be monoalkylated.[8,10] The idea was originally based on the *in vivo* reactions of phosphoenol pyruvate with carbon dioxide[11a] or with sugar aldehydes,[11b] and more recently on the cleavage of α,α-disubstituted β-ketophosphonium salts with Grignard reagents to give ketones.[12] We now report the successful utilization of enol phosphorylated species along these lines.[13]

Results and Discussion

Our initial results involved the cleavage of enol-phosphorylated derivatives of the 1,2-diphenylethylene system (Table I) with phenylmagnesium bromide or phenyllithium. The enol triphenylphosphonium chloride **6**, from α-chlorobenzyl phenyl ketone (**2**) and TPP,[6d] reacts with phenylmagnesium bromide or phenyllithium to give the enolate **7**. Biphenyl and TPP, formed as by-products, may arise *via* tetraphenylphosphonium halide and pentaphenylphosphorane[14] intermediates, as postulated in β-ketophosphonium salt reactions with Grignard reagents.[12]



The enol phosphonium bromide **11**, derived from **10**, reacted similarly.



(1) This investigation was supported by Grant No. 19,664 from the National Science Foundation. This is part 22 of the series Organophosphorus Chemistry. Taken in part from R. K. Crouch, Ph.D. Thesis, Yeshiva University, 1972. Presented in part at the Heteroatom Chemistry Meeting, London, Ontario, Sept 1970.

(2) To whom correspondence should be addressed.

(3) (a) F. W. Lichtenthaler, *Chem. Rev.*, **61**, 607 (1961); (b) P. A. Chopard, V. M. Clark, R. F. Hudson, and A. J. Kirby, *Tetrahedron*, **21**, 1961 (1965).

(4) (a) I. J. Borowitz, M. Anschel, and S. Firstenberg, *J. Org. Chem.*, **32**, 1723 (1967); (b) I. J. Borowitz, S. Firstenberg, E. W. R. Casper, and R. K. Crouch, *ibid.*, **36**, 3282 (1971).

(5) I. J. Borowitz and R. K. Crouch, *Phosphorus*, in press.

(6) (a) I. J. Borowitz, K. Kirby, P. E. Rusek, and E. W. R. Casper, *J. Org. Chem.*, **36**, 88 (1971); (b) A. J. Speziale and R. D. Partos, *J. Amer. Chem. Soc.*, **85**, 3312 (1963); (c) R. D. Partos and A. J. Speziale, *ibid.*, **87**, 5068 (1965); (d) I. J. Borowitz, P. E. Rusek, and R. Virkhaus, *J. Org. Chem.*, **34**, 1595 (1969).

(7) (a) H. O. House and B. M. Trost, *ibid.*, **30**, 1341, 2502 (1965); (b) H. O. House, *Rec. Chem. Progr.*, **28**, 99 (1967); (c) H. O. House and C. J. Blankley, *J. Org. Chem.*, **32**, 1741 (1967); (d) H. O. House and T. M. Bare, *ibid.*, **33**, 943 (1968).

(8) G. Stork and P. F. Hudrlik, *J. Amer. Chem. Soc.*, **90**, 4462, 4464 (1968).

(9) H. O. House, L. J. Czuba, M. Gall, and H. O. Olmstead, *J. Org. Chem.*, **34**, 2324 (1969).

(10) H. O. House, M. Gall, and H. O. Olmstead, *ibid.*, **36**, 2361 (1971).

(11) (a) J. L. Graves, B. Vennesland, M. F. Utter, and R. J. Pennington, *J. Biol. Chem.*, **223**, 551 (1956); (b) P. R. Srinivasan and D. B. Sprinson, *ibid.*, **234**, 716 (1959).

(12) T. Mukaiyama, R. Yoda, and I. Kuwajima, *Tetrahedron Lett.*, 23 (1969).

(13) I. J. Borowitz, E. W. R. Casper, and R. K. Crouch, *ibid.*, 105 (1971).

(14) (a) G. Wittig and G. Geissler, *Justus Liebigs Ann. Chem.*, **580**, 44 (1953); (b) G. Wittig and M. Rieber, *ibid.*, **562**, 187 (1949).

TABLE I

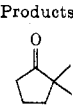
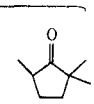
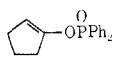
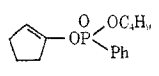
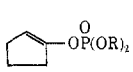
CLEAVAGE AND SUBSEQUENT REACTIONS OF PHOSPHORYLATED 1,2-DIPHENYLETHYLENES OR 11

		Yield, %				
Compd	Conditions	Ketone	Methyl ketone	Biphenyl	$OPPh_3$	PPh_3
6	1. PhMgBr,[a] THF[b] 2. CH_3I added[b]	1	36	16		100
6	1. PhLi, THF[b] 2. CH_3I added[c]	4	86	64		100
5	1. PhMgBr,[a] THF[b] 2. CH_3I added[b]	1	85		98	
11	1. PhMgBr, THF (25°) 2. CH_3I added, 25°, 16 hr	27	46	34[d]	95[d]	

[a] Two equivalents. [b] Reflux 12 hr. [c] Reflux 5 hr. [d] From the acidification of the enolate in a separate experiment. Oxidation of anticipated PPh_3 may have occurred during work-up.

TABLE II

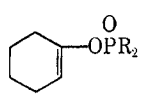
CLEAVAGE–ALKYLATION OF CYCLOPENTENYL DERIVATIVES WITH METHYL IODIDE[a,b]

			Products				
Compd	Organolithium (1 equiv)	Solvent					
 15	CH_3Li	Glyme	1	77 (76)[c]	7	12	3
	CH_3Li	THF	1	74 (72)[c]	7	15	3
 16	n-C_4H_9Li	Glyme	5	64	16	9	6
 17, R = C_2H_5	CH_3Li	Glyme	12	78	4	6	0
18, R = i-C_3H_7	CH_3Li	Glyme	14	62	9	12	3

[a] Cleavage for 5 min at room temperature; alkylation at 0° and quenched after 1 min. [b] All samples analyzed by vpc at 110° on 20% SE-30. Retention times: cyclopentanone, 2.3 min; 2-methylcyclopentanone (3.3); 2,2-dimethylcyclopentanone (3.8); 2,5-dimethylcyclopentanone (4.3). [c] Yield by vpc calibration curve.

TABLE III

CLEAVAGE–ALKYLATION OF CYCLOHEXENYL DERIVATIVES WITH METHYL IODIDE[a,b]



				Products		
Compd	Organolithium (equiv)	Cleavage temp, °C	Solvent	55	1	28
19, R = Ph	n-C_4H_9Li (1.1)	0	Glyme–DMSO (2:1)	1.6	90.4 (86)[c]	8.0
20, R = Ph, OC_4H_9	CH_3Li (1.0)	25	Glyme	14	81 (80)[c]	5
21, R = OC_2H_5	CH_3Li (1.0)	25	Glyme	32	63	5
21	CH_3Li (2.0)	25	Glyme	13	79 (75)[c]	8
22, R = O-i-C_3H_7	CH_3Li (1.0)	25	Glyme	12	86	2

[a] Cleavage for 5 min. Alkylating solutions at 0° and alkylation step terminated after 5 min. [b] Vpc conditions for product analysis at 130° on 20% SE-30. Retention times: cyclohexanone (3.3 min); 2-methylcyclohexanone (4.5); 2,2-dimethylcyclohexanone (5.5); 2,6-dimethylcyclohexanone (6.0, genuine sample used). [c] Calibration curve (vpc).

The cleavage of vinyl phosphinate **5**, which was obtained from reaction of ethyl diphenyl phosphinite (**4**) with **2** (or **3**), phosphonates, or phosphates, was found to be best performed with methyl- or butyllithium in glyme to give a lithium enolate and a phosphine oxide, phosphinate, or phosphonate. Monoalkylation was achieved by rapid reaction of the enolate, which was added to alkyl iodide in glyme containing a small amount of dimethyl sulfoxide or hexamethylphosphoramide.[15]

The formation and the subsequent methylation of the lithium enolates of cyclopentanone and cyclohexanone are given in Tables II and III. Insignificant amounts of unalkylated ketone are obtained from the vinyl phosphinates **15**[5] and **19**,[4b] while the vinyl phosphates **17**,[4b] **18**, **21**, and **22** give these undesired by-products in greater yield. This may be due to a side reaction of the alkyllithium which displaces an alkoxide group from phosphorus.[16] The use of the diisopropyl vinyl phosphate **22** gives only slightly

(15) (a) P. Hudrlik, Ph.D. Thesis, Columbia University, 1968; (b) T. A. Spencer, R. W. Britton, and D. S. Watt, *J. Amer. Chem. Soc.*, **89**, 5727 (1967); (c) P. A. Tardella, *Tetrahedron Lett.*, 1117 (1969).

(16) K. Sasse, Ed., "Organische Phosphorverbindungen, Methoden der Organischen Chemie (Houben-Weyl)," Vol. 12/1, Georg Thieme Verlag, Stuttgart, 1963, pp 32–43.

TABLE IV

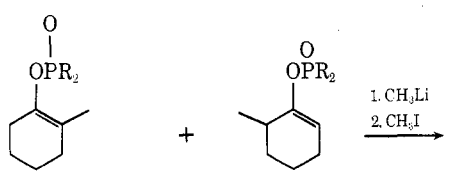
CLEAVAGE–ALKYLATION OF 2-METHYLCYCLOHEXENYL DERIVATIVES WITH METHYL IODIDE[a]

Compd	Organolithium (equiv)	Cleavage conditions	Solvent	Alkylation Temp, °C	Alkylation Time, min	Products 1	28	29	30	31
27	n-C_4H_9Li (1.0)	c, d	Glyme	25	2	2	91.5 (87)[b]	0	6.5	0
27	n-C_4H_9Li (1.3)	c	Glyme–DMSO (2:1)	0	5	25	60.8	0	14	0.2
26	n-C_4H_9Li (1.0)	e	Glyme	0	2	7	80	2	11	0
23	CH_3Li (1.0)	e	Glyme	0	1	18	76	3	3	0
24	CH_3Li (1.0)	e	Glyme	0	1	17	0	76 (75)[b]	3	4
25	n-C_4H_9Li (1.0)	f	Glyme	0	1	13	60	5	22	0

[a] Analysis by vpc as in Table III. Retention time **30** (7.0 min), **31** (8.0). [b] By vpc calibration curve. [c] At 0° for 1 hr. [d] The use of C_6H_5Li gave the product ratio 15:63 (**28**):2:15 (**30**):5. [e] At 25° for 20 min. [f] At 50° for 24 min.

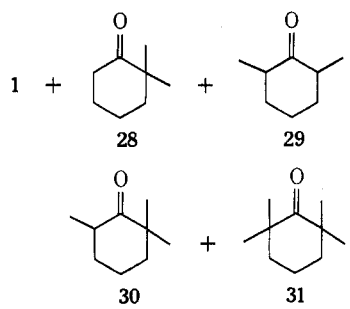
less cyclohexanone **55** than does the less hindered diethyl vinyl phosphate **21**.

The cleavage and methylation of the more and the less substituted isomeric vinyl phosphates of 2-methylcyclohexanone (**23–25**) and of other vinyl phosphorylated derivatives of the more substituted isomer (**26**, **27**[5]) are given in Table IV. The data indicates that butyllithium is more effective than is phenyllithium in the cleavage step and that an excess (0.3 equiv) of butyllithium results in overalkylation even though less ketone **1** is obtained.



23, R = OC_2H_5
25, R = O-*i*-C_3H_7
26, R = Ph, OC_4H_9
27, R = Ph

24, R = OC_2H_5



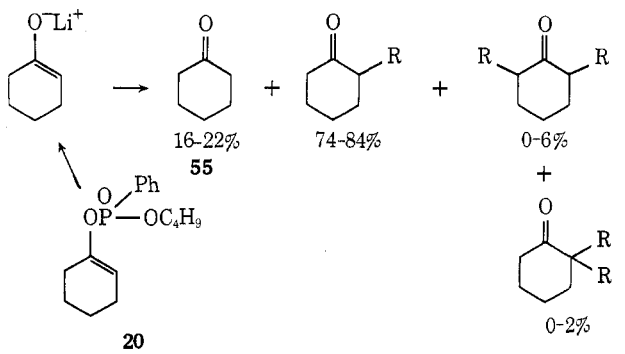
28 **29** **30** **31**

The alkylation of the lithium enolate of cyclohexanone generated from **20** with groups larger than methyl is summarized in Table V.

Reasonable yields of monoalkylated product are obtained with alkyl iodides although longer reaction times (1–4 hr) and elevated temperatures relative to methylation are required. Little or no dialkylation is noted for groups larger than ethyl.

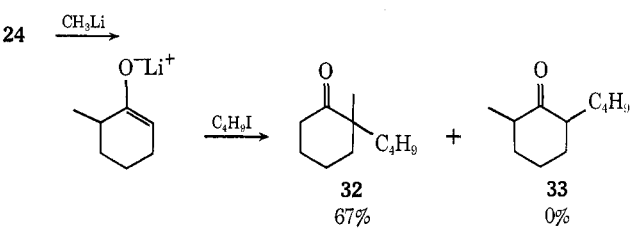
Reaction of the lithium enolate of cyclohexanone, formed under kinetic control conditions[17] with butyl iodide, also gives mainly monoalkylation.

(17) (a) H. O. House and V. Kramer, *J. Org. Chem.*, **28**, 3362 (1963); (b) the reagent of choice for kinetically controlled alkylations is now lithium diisopropylamide.[10]



20

An attempt to butylate the less substituted enolate formed from **24** gives the 2,2 isomer **32**[18] as the major product rather than **33**, the expected product. Thus



32 67% **33** 0%

with alkylations considerably slower than methylation, equilibration of the less stable enolate of 2-methylcyclohexanone to the more stable one can occur faster than the alkylation. Thus far only methylation and benzylation[10] occur primarily on the less substituted side.

Extension of the cleavage–alkylation and direct alkylation sequences to cycloheptanone systems are given in Table VI. Little or no polyalkylation is observed for groups larger than methyl in the absence of excess base.

Several acyclic systems are thus monoalkylated. The vinyl phosphonate **37**[4b] of acetone is monobutylated to give 2-heptanone (**38**), and the dimethyl vinyl phosphate of butyraldehyde (**39**)[4b] is similarly converted to 2-methylbutyraldehyde (**40**).

α-Alkyl-α′-bromo Ketones.—The synthesis of less substituted vinyl phosphates such as **24** depends upon the availability of α-alkyl-α′-halo ketones such as 2-methyl-6-bromocyclohexanone (**42**). In principle pyr-

(18) P. Nedenskov, W. Taub, and D. Ginsburg, *Acta Chem. Scand.*, **12**, 1405 (1958).

TABLE V

ALKYLATION OF CYCLOHEXANONE LITHIUM ENOLATE WITH VARIOUS ALKYL HALIDES

Precursor of enolate	Alkyl halide	Solvent	Time, hr	Temp, °C	Vpc conditions	Products: Cyclohexanone	2-Alkylcyclohexanone	2,2- or 2,6-Dialkylcyclohexanone
Cyclohexanone[a]	n-C_4H_9I	Glyme	4	90	b	18	74	2 (**56**)[h] 6 (**57**)[i]
20[e]	C_2H_5I	Glyme	0.5	50	c	22	76	2
20	i-C_3H_7I	Glyme–HMPA (2:1)	20	90	d	16	84	0
20	n-C_4H_9I	Glyme	4	90	b	22	78	0
20	n-C_4H_9I	Glyme–HMPA (2:1)	4	90	b	17	83	0
20	n-C_4H_9Br	Glyme–HMPA (2:1)	20	90	b	20	80 (67)[f]	0
						2-Methylcyclohexanone	2-Methyl-2-butylcyclohexanone	
24	n-C_4H_9I	Glyme	24	90	g	31 (1)	69 (**32**)	0

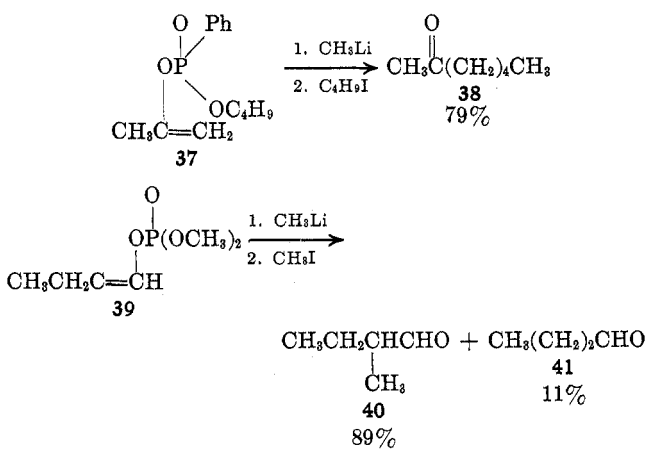
[a] Reacted with $LiCPh_3$ (1.0 equiv) for 1 min at 0°. [b] At 160°. [c] At 145°. [d] At 150°. All vpc work done on 20% SE-30 on Chromosorb W (10 ft × 0.25 in.) except for mixture from **24** (done on 10% SE-30). [e] Cleavage of **20** or **24** was done with CH_3Li (1 equiv) at 25° for 15 min. [f] Distilled yield. [g] At 140°. [h] 2,2-Dibutylcyclohexanone. [i] 2,6-Dibutylcyclohexanone.

TABLE VI

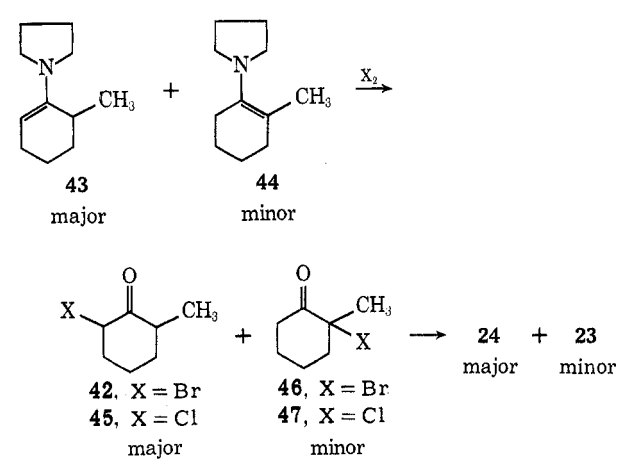
ALKYLATION OF CYCLOHEPTANONE LITHIUM ENOLATE WITH VARIOUS ALKYL HALIDES

Precursor of enolate	Alkyl halide	Solvent	Time, hr	Temp, °C	Vpc conditions	Products: Cycloheptanone	2-Alkylcycloheptanone
Cycloheptanone[a]	n-C_4H_9I	Glyme	16	90	b	42 (35)	58 (**36**)
Diethyl cycloheptenyl phosphate (**34**)	n-C_4H_9I	Glyme–HMPA (2:1)	16	90	b	24	76 (**36**)
34	n-C_4H_9Br	Glyme–HMPA	96	90	b	51	49 (**36**)
34	$CH_2{=}CH(CH_2)_2Br$	Glyme–HMPA	88	90	c	39	61
34	CH_3I	Glyme–HMPA	0.05	25	d	16	80[e]

[a] Reacted with $LiCPh_3$ (1.0 equiv) for 5 min at 0°. [b] At 165°. [c] Programmed from 150° to 200° at 4°/min. Retention times: cycloheptanone (4.5 min); 2-(3′-butenyl)cycloheptanone (13.5). [d] At 160°. All vpc work on 20% SE-30 column as in Table V. [e] Also 2% dimethylcycloheptanone (2,2- or 2,6-) and 2% 2,2,6-trimethylcycloheptanone.



rolidino-2-methylcyclohexene, which exists as a 9:1 mixture of **43** and **44**,[19] should be convertible to **42** or **45**, and little **46** or **47**, by halogenation.[20a] In practice, a number of halogenation procedures on **43** and **44** involving bromine, sulfuryl chloride, N-bromosuccinimide, or N-chlorosuccinimide give primarily **46** or **47** and little of the desired **42** or **45**. Chlorination gives **45** and **47**.[20b,c] Bromination of **43** and **44** in acetic acid,[21] however, reproducibly gives **42**. Reaction of **42** with triethyl phosphite gives mainly **24** and very little **23**. Attempted debromination of **42** gives 2-methyl-2-cyclohexenone (**48**) and not 2-methyl-5-cyclohexenone (**49**).[22]



We find that the bromination of 2-methylcyclohexanone (in methanol) or bromination of its ethylene glycol ketal (**50**) gives mainly **46** and not **42**, contrary to

(19) (a) M. E. Kuehne, *J. Amer. Chem. Soc.*, **81**, 5400 (1959); (b) H. O. House and M. Schellenbaum, *J. Org. Chem.*, **28**, 34 (1963).

(20) (a) Originally suggested by Professor G. Stork; (b) I. J. Borowitz, unpublished results; (c) L. Futrell, unpublished results, Yeshiva University.

(21) M. Kuehne and T. J. Giacobbe, *J. Org. Chem.*, **33**, 3359 (1968).

(22) See E. W. Warnhoff, *ibid.*, **27**, 4587 (1962), for related phenomena.

previous work.[23] Attempts to brominate 2-methyl-6-carboxycyclohexanone (**51**)[24] give mixtures of **46** and **42** at best.

Attempts to extend enamine brominations to other unsymmetrical ketones are in progress.

Experimental Section[25]

All solvents used were dried by distillation from calcium hydride, phosphorus pentoxide, or lithium aluminum hydride. Most reactions, including all alkylations, were conducted under prepurified nitrogen. Organic solutions were dried over anhydrous magnesium sulfate. Most of the vinyl phosphorylated species have been described,[3-6] as have their halo ketone precursors.[5,6a,6d]

Butyl 1-cyclopentenyl phenylphosphonate (**16**), 82% from the neat reaction of dibutyl phenylphosphonate (**52**) and 2-chlorocyclopentanone at 80° for 24 hr, had bp 135° (0.1 mm); ir (neat) 6.0 μ; nmr ($CDCl_3$) τ 7.4–9.2 (m, 13, CH_2, CH_3), 6.10 (m, 2, OCH_2), 4.85 (m, 1, vinyl H), 2.0–2.8 (m, 5, phenyl); mass spectrum[26] (70 eV) *m/e* 280.1239 (calcd 280.1228). *Anal.* Calcd for $C_{15}H_{21}O_3P$: C, 64.24; H, 7.55. Found: C, 63.97; H, 7.69.

Butyl 1-cyclohexenyl phenylphosphonate (**20**), 86% from **52** and 2-chlorocyclohexanone in $CHCl_3$ at reflux for 36 hr, had bp 130° (0.05 mm); ir (neat) 6.0 μ; nmr ($CDCl_3$) τ 4.64 (m, 1, vinyl) and other peaks as for **16**; mass spectrum[26] (70 eV) *m/e* 294.1411 (calcd 294.1385). *Anal.* Calcd for $C_{16}H_{23}O_3P$: C, 65.28; H, 7.88. Found: C, 63.48 (could not be improved); H, 8.08.

Butyl 1-(2-methyl)cyclohexenyl phenylphosphonate (**26**), 91% from **52** and 2-methyl-2-chlorocyclohexane (**47**) in $CHCl_3$ at reflux for 90 hr, had bp 148–150° (0.1 mm); ir (neat) 6.05 μ. *Anal.* Calcd for $C_{17}H_{25}O_3P$: C, 66.18; H, 8.17. Found: C, 66.08; H, 8.25.

The following vinyl phosphates were synthesized from the appropriate halo ketone and triisopropyl phosphite (**53**) in 2-propanol. Their nmr spectra exhibited τ 7.5–8.2 (CH, CH_2), 8.6–8.7 (d, CH_3), 5.35–5.46 (m, OCH).

Diisopropyl cyclopentenyl phosphate (**18**), 49% from **53** and 2-chlorocyclopentanone (100°, 18 hr), had bp 62–64° (0.05 mm); ir (neat) 6.05 μ; nmr ($CDCl_3$) τ 4.75 (m, 1, vinyl). *Anal.* Calcd for $C_{11}H_{21}O_4P$: C, 53.21; H, 8.53. Found: C, 53.03; H, 8.62.

Diisopropyl cyclohexenyl phosphate (**22**), 81% from **53** and 2-chlorocyclohexanone (25°, 18 hr), had bp 95–97° (0.1 mm); ir (neat) 5.95 μ; nmr ($CDCl_3$) τ 4.55 (m, 1, vinyl). *Anal.* Calcd for $C_{12}H_{23}O_4P$: C, 54.94; H, 8.84. Found: C, 54.71; H, 8.80.

Diisopropyl 1-(2-methyl)cyclohexenyl phosphate (**25**), 57% from **53** and **47** (90°, 48 hr), had bp 108–110° (0.03 mm); ir (neat) 6.0 μ; nmr ($CDCl_3$) τ 7.6–8.5 (m, 11, CH_2, vinyl CH_3). *Anal.* Calcd for $C_{13}H_{25}O_4P$: C, 56.51; H, 9.09. Found: C, 56.75; H, 9.07.

Diethyl 1-(6-methyl)cyclohexenyl phosphate (**24**), 78% from crude 2-methyl-6-bromocyclohexanone, **42** (*ca.* 0.15 mol), and triethyl phosphite (25 g, 0.162 mol) in $CHCl_3$ at reflux for 24 hr, had bp 100–103° (0.07 mm); ir (neat) 6.0 μ; nmr (CCl_4) τ 5.82 (m, 4, OCH_2), 4.58 (m, 0.85–1, vinyl H), 8.9 (d, 3, CH_3CH, ^3J = 7 Hz); vpc (5% Carbowax on Chromosorb W, Teflon–aluminum column) one peak with retention time of 12.2 min at *ca.* 120° (temperature-programmed run). However, the isomeric **23** or a 1:1 mixture of **23** and **24** gave the same peak, *i.e.*, no separation. *Anal.* Calcd for $C_{11}H_{21}O_4P$: C, 53.22; H, 8.53. Found: C, 53.07; H, 8.77.

Diethyl 1-(2-methyl)cyclohexenyl phosphate (**23**), 69% from TEP and 2-methyl-2-chloro (or bromo) cyclohexanone,[4a] had bp 90–92° (0.1 mm) [lit.[4a,27] bp 91–92° (0.1 mm)]; ir (film) 5.88 μ; nmr ($CDCl_3$) τ 8.32 (broad s, 4.6, includes vinyl CH_3) and other peaks as for **24**.

General Procedure for the Cleavage–Alkylation of Enol Phosphorylated Species.—To the enol phosphorylated species (0.01 mol) in glyme (50 ml) containing a trace of triphenylmethane,[7] alkyl- or aryllithium (0.01 mol unless otherwise specified, 0.50–2.5 *M* in ether or hexane) was added under nitrogen by syringe until a red color persisted. The solution was stirred for the length of time specified and at the given temperature in the tables. The resultant enolate was then added under nitrogen to a solution of the alkylating agent in glyme, glyme–HMPA, or glyme–DMSO (10 ml of glyme, 5 ml of DMSO or HMPA) at the specified temperature. After a given reaction time, hydrochloric acid (1 *N*, 50 ml, 0.05 mol) was added. The organic layer, combined with diethyl ether extracts (3 × 50 ml) of the aqueous layer, was washed with saturated $NaHCO_3$ and dried ($MgSO_4$) and the solvent was distilled at 760 mm to give a residue which was dissolved in hexane and analyzed by vpc. Phosphinate or phosphonate by-products were removed during the acidic work-up while phosphine oxides either remained as hexane-insoluble residue or could be removed by filtration through alumina (especially for preparative scale reactions). The identity of the alkylated products was either assumed from known vpc retention times,[15a] by comparison with genuine samples or as follows. The vpc product analyses assumed equal thermal conductivity detector response for the parent and alkylated ketones in a reaction mixture. This commonly used procedure was shown to be valid or to involve small error in a number of cases by comparison with known samples of unalkylated and alkylated ketone. The yield of the major product in some runs was also estimated by vpc calibration curves using known samples of 2-methylcyclohexanone, 2,6-dimethylcyclohexanone, 2-methylcycloheptanone, 2-ethylcyclohexanone,[19a] and 2-isopropylcyclohexanone.[28]

Reactions of Enol Triphenylphosphonium Bromide 11 and Related 1,2-Diphenylethylene Phosphorylated Species.—The cleavage of **11** with phenylmagnesium bromide followed by methylation gave methyldiphenylacetophenone (**14**, 46%): mp 90–92° (lit.[29] mp 91–92°); ir ($CHCl_3$) 5.99 μ; uv max (95% C_2H_5OH) 250 nm (log ϵ 4.05) [lit.[30] uv max 245 (4.0)]; nmr ($CDCl_3$) τ 2.82 (s, 3, CH_3), 2.25, 2.35 (d, *ca.* 2, ortho H of PhCO), 2.7 (m, *ca.* 13, phenyl H); mass spectrum (70 eV) *m/e* 286 ($M\cdot^+$), 271 ($PhCOC^+Ph_2$), 183 (Ph_2C^+OH), 166 (Ph_2C^+), 105 ($PhCO^+$), 77 ($C_6H_5^+$), metastable peak at *ca.* 60 for 105 → 77.

Similar reaction of enol phosphonium salt **6**[6d] or vinyl phosphinate **5** gave α-methylbenzylphenyl ketone (**9**): ir ($CHCl_3$) 5.94 μ; nmr ($CDCl_3$) τ 5.34 (q, 1, methine H, ^3J = 7 Hz), 8.49 (d, 3, CH_3, ^3J = 6.9 Hz); mass spectrum (70 eV) *m/e* 210 ($M\cdot^+$), 195 ($PhCOCH^+Ph$), 178 ($PhCH_2^+$), 105 ($PhCO^+$, $PhCH^+CH_3$), 91, 77. No dimethylated ketone was found.

2-Butylcyclohexanone (**54**).—The cleavage of butyl cyclohexenyl phenylphosphonate (**20**, 0.05 mol) with methyllithium at 25° for 15 min, followed by reaction with butyl iodide in glyme–HMPA for 4 hr at 90°, gave 2-butylcyclohexanone (**54**)–cyclohexanone (**55**) in 80:20 ratio (vpc retention time 9.0 min, 1.5 min at 160° on 20% SE-30 on Chromosorb W in a 10 ft × 0.25 in. column). Distillation gave **54** (5.2 g, 0.032 mol, 64%): bp 89–92° (12 mm) [lit.[28] bp 86–96° (15–20 mm)]; vpc (as above) 99% one peak; 2,4-DNP (orange needles) mp 110–112° (lit.[28] mp 112–113°).

2-Methyl-2-butylcyclohexanone (**32**).—Cleavage and alkylation of **24** (Table V) with methyllithium and butyl iodide gave 2-methyl-2-butylcyclohexanone (**32**): vpc at 165° (20% SE-30) 22–3% **1**, 65–69% **32**, 0–13% **24** depending upon run; ir (film) 5.87 μ, similar but nonidentical spectrum with that of **33**; nmr (CCl_4) τ 7.8, 8.5–8.9 (m, *ca.* 15), 9.3, 9.4 (part of butyl methyl), and 9.02, which was shifted to 9.5 (s, 3, C_2CH_3) by 0.033 equiv of $Pr(DPM)_3$.[31] The 2,4-DNP of a vpc-collected sample had mp 142–144° (lit.[18] mp 144°).

2-Methyl-6-butylcyclohexanone (**33**).—To 2-methyl-6-carboethoxycyclohexanone (4.60 g, 0.025 mol) in dry toluene (30 ml) was added NaH [0.60 g, 0.025 mol, washed with petroleum ether

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(25) The instrumental techniques used have been recorded.[4b,6a] Mass spectra were recorded on Hitachi RMU-6 mass spectrometers at the Einstein Medical College or at Columbia University.

(26) High-resolution mass spectra were done by R. Foltz, Battelle Memorial Institute, Columbus, Ohio, on an MS-9 mass spectrometer under NIH contracts 69-2226 and 71-2483.

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(30) (a) H. Rinderknecht, *J. Amer. Chem. Soc.*, **73**, 5770 (1951); (b) M. J. Kamlet, Ed., "Organic Electronic Spectral Data," Vol. 1, Interscience, New York, N. Y., 1960.

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(bp 30–60°) to remove oil]. The mixture was heated at reflux for 3 hr after the initial exothermic reaction subsided, and then cooled. Butyl bromide (3.7 g, 0.027 mol) in toluene (10 ml) was added over 10 min and the resultant mixture was heated at reflux for 17 hr. The usual work-up gave a yellow oil [3.9 g crude, vpc (at 240° on 20% SE-30) 62% alkylated β-keto ester, 38% starting β-keto ester]. The crude product was hydrolyzed with NaOH (4.0 g, 0.1 mol) in C_2H_5OH–H_2O (100 ml each), acidified with dilute HCl, and extracted with ether to give 2-methyl-6-butylcyclohexanone (*ca.* 2.3 g, 0.007 mol, 29%): bp 85° (2.5 mm); ir (film) 5.87 μ; nmr (CCl_4) τ 7.5–9.35 (m, 20) with apparent doublet at 9.06 (J = 6 Hz) which was shifted to 9.64 (d, 3, CH_3CH, J = 6 Hz) with 0.038 equiv of $Pr(DPM)_3$. In comparison the nmr (CCl_4) of 2-methylcyclohexanone has τ 9.06 (d, 3, CH_3, J = 6 Hz). No separation of **32** and **33** by vpc was noted on 20% SE-30 (175–217°) or 5% Carbowax (100–135°) columns under isothermal or temperature-programmed conditions. *Anal.* Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.40; H, 11.94. The 2,4-DNP of **33** formed with difficulty (in contrast to that of **32** which formed readily) and was an oil: uv max (95% C_2H_5OH) 363 and 228 nm; ir (film) 6.15 μ (C=N); tlc (silica gel HF_{254}) R_f 0.3 (ether–hexane) while 2,4-DNPH had R_f 0; uv max (95% C_2H_5OH) 350, 260 nm; nmr ($CDCl_3$) τ −1.2 (s, 1, NH), 0.8 (d, 1, aryl H_o), 1.6–2.1 (AB quartet, 2, aryl $H_{a,b}$), 6.8–9.3 (m, 20).

2-Butylcycloheptanone (**36**)[32] was collected by vpc (on 20% SE-30) from the cleavage–alkylation of **34**[4b] (Table VI): mass spectrum (20 eV) m/e (rel intensity) 168 ($M\cdot^+$, 37), 153 ($M - CH_3$, 3), 112 [$CH_2{}^+(CH_2)_2CH\cdot$–C_4H_9, 56], 111 [$^+O{\equiv}CC(C_4H_9){=}CH_2$, 33], 97 ($C_6H_9O$, 100), 55 ($^+O{\equiv}CC{=}CH_2$, 89); calcd M + 1 for $C_{11}H_{20}O$, 12.1; found, 12.2.

2-Methylbutyraldehyde (**40**) was separated from butyraldehyde [out of the mixture resulting from the cleavage (0°, 1 min), alkylation (25°, 1 min) of **39**] by its greater solubility in ether. It was identified by its vpc retention time (5.1 min at 85° on 20% SE-30) which was identical with that of a genuine sample and by conversion to its 2,4-DNP: mp 120–121°; mmp 121–122° with that of a genuine sample (lit.[33] mp 120°).

(32) W. von E. Doering and C. F. Hiskey, *J. Amer. Chem. Soc.*, **74**, 5688 (1952).

(33) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 5th ed, Wiley, New York, N. Y., 1967, p 320.

2-Heptanone (**38**).—The lithium enolate of acetone, generated from the butyl phenylphosphonate **37**, was alkylated with butyl iodide for 3 hr at 25° to give **38** (79% as determined by a vpc calibration curve using genuine samples). No polyalkylated material was detected. The vpc of **38** had a retention time of 5.8 min at 130° on 20% SE-30. The yield of recovered acetone could not be determined because of its nonseparation from other volatile components (vpc).

2-Methyl-6-bromocyclohexanone (**42**).—To pyrrolidino-6-methylcyclohexene (**43**, 25.0 g, 0.15 mol) in $CHCl_3$ (200 ml) and glacial acetic acid (90 ml), cooled to 0–5° in a salt–ice bath, bromine (28.0 g, 0.15 mol) in $CHCl_3$ (50 ml) was added dropwise with stirring under nitrogen. The reaction temperature was kept below 5° during the addition and for another 10 min, water (200 ml) was added and the reaction mixture was poured into saturated $NaHCO_3$ solution (400 ml). The organic layer was washed with water (3 × 200 ml), dried ($MgSO_4$), and usually directly converted to vinyl phosphate **24**. Removal of the solvent at 25° *in vacuo* gave a dark red oil: nmr (CCl_4) τ 8.91 (d, *ca.* 3, CH_3, J = 6.5 Hz), 7.0–8.4 (m, 7, CH_2), 5.22 (m, *ca.* 1, CHBr). Yields were *ca.* 80% of mixtures of 8–9 parts of **42** and 1–2 parts of 2-methyl-2-bromocyclohexanone (**46**). Rearrangement of **42** to **46** occurred in part upon attempted vpc and slowly at 25° (complete conversion in 24 hr). Reaction of **42** with lithium bromide, lithium carbonate, dimethylformamide, or collidine gave only 2-methylcyclohexenone, 2,4-DNP mp 208° (lit.[34] mp 207.5–208.5°).

Registry No.—**5**, 30758-39-5; **6**, 30758-40-8; **9**, 2042-85-5; **11**, 26709-97-7; **14**, 36504-01-5; **15**, 30758-45-3; **16**, 36504-02-6; **17**, 30842-23-0; **18**, 36504-03-7; **19**, 30758-41-9; **20**, 30758-44-2; **21**, 4452-32-8; **22**, 36504-04-8; **23**, 30908-58-8; **24**, 30908-59-9; **25**, 36504-06-0; **26**, 36547-04-3; **27**, 30758-42-0; **32**, 1197-78-0; **33**, 36504-08-2; **33** DNP, 36504-09-3; **34**, 31327-27-2; **36**, 36504-11-7; **42**, 36504-12-8; cyclohexanone lithium enolate, 21300-30-1; 2-methylcyclohexanone lithium enolate, 13670-83-2; cycloheptanone lithium enolate, 36504-15-1.

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Chirality and Structure of Organosilicon Radicals

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Pyramidal structure for triorganosilyl radicals ($R_3Si\cdot$) in general is indicated by chirality studies on five optically active organosilicon systems containing asymmetric silicon. Reactions of five different optically active silanes, R_3Si^*H, with carbon tetrachloride, catalyzed by benzoyl peroxide, gave optically active R_3Si^*Cl compounds. Progressively greater dilution of the carbon tetrachloride with benzene or cyclohexane demonstrated the capacity of the α-NpPhMeSi·* radical to invert. Also, for reasons presently unknown $Ph_3SiSi^*(Ph)(Me)H$ gave optically inactive $Ph_3SiSi^*(Ph)(Me)Cl$.

Recent studies by Brook[1] and Kumada[2] have provided evidence that the α-naphthylphenylmethylsilyl radical as generated in reactions 1 and 2 below is chiral and nonplanar. In these studies R_3Si^*Cl is optically active α-NpPhMeSi*Cl.

$$R_3Si^*H + CCl_4 \xrightarrow[\Delta]{Bz_2O_2} R_3Si^*Cl + CHCl_3 \quad (1)$$

$$R_3Si^*COCH_3 + h\nu \longrightarrow R_3Si\cdot^* + \cdot COCH_3 \xrightarrow{CCl_4} R_3Si^*Cl + CH_3COCl \quad (2)$$

In both reactions the optically active organosilicon reactants gave the product chlorosilane, R_3Si^*Cl, with *retention* of configuration. For reactions 1 and 2, respectively, optical purities of product R_3Si^*Cl were 86 and 64%.

However, both of the above studies were limited to generation and reaction of the same radical, α-NpPhMeSi·, and we wish now to report results which demonstrate (a) chirality for a wide variety of monosilane radicals; (b) nonchirality or rapid inversion for a disilane radical; (c) capacity of the α-NpPhMeSi·* radical to invert under conditions of progressively greater dilution of the CCl_4 in reaction 1 by benzene and cyclohexane.

Results for reaction 1 using a wide variety of R_3Si^*H compounds and pure CCl_4 as solvent–reactant are reported in Table I. References listed in Table I

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