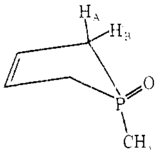
(17) After 24 h at room temperature there was a slight decrease in the amount of A and a comparable increase in the amount of acetone.

(18) R. S. Macomber, *Synth. Commun.*, **7(6)**, 405 (1977).

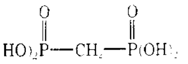
(19) E. J. Eisenbraun, R. N. Morris, and G. Adolphen, *J. Chem. Educ.*, **47**, 710 (1970).

(20) Analogous compounds show very similar chemical shifts and P–H coupling constants: ii [K. Moedritzer and P. A. Berger, *J. Org. Chem.*, **42**, 2023 (1977)]; iii and iv [Sadtler Research Labs NMR Standard Spectra 7770, 7771]



δ_A 2.59 (J_{PA} = 14 Hz)
δ_B 2.47 (J_{PB} = 8 Hz)

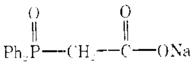
ii



$$(HO)_2P(=O)—CH_2—P(=O)(OH)_2$$

δ_{CH_2} 2.61 ($^2J_{PH}$ = 21 Hz)

iii



$$Ph_2P(=O)—CH_2—C(=O)—ONa$$

δ_{CH_2} 3.59 ($^2J_{PH}$ = 14 Hz)

iv

(21) This technique has been used to isolate salts of other phosphonic acids: R. Rabinowitch, *J. Org. Chem.*, **28**, 2975 (1963).

(22) Compound **5b** was found to form a phosphonic anhydride under certain hydrolysis conditions: R. C. Elder, L. R. Florian, E. R. Kennedy, and R. S. Macomber, *J. Org. Chem.* **38**, 4177 (1973).

(23) The dicyclohexylamine salt of **7a** is stable in water, suggesting that the hydrolytic ring opening is acid catalyzed.

(24) Less than 20 mg of *m*-chlorobenzoic acid is extracted into the water.

(25) Elemental analysis performed by Integral Microanalytical Labs.

Procedure for the Permethylation of Ketones Using Potassium Hydride and Methyl Iodide

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The classical method for the synthesis of permethylated ketones is sequential reaction of the ketone with portions of sodamide and methyl iodide.[1] More recent methods utilize such bases as sodium alkoxides[2] or sodium hydride.[3] In most cases, the overall yield for the replacement of all enolizable hydrogens does not exceed 50%.

We recently required a sample of 2,2,6,6-tetramethylcyclohexanone. The excellent procedure discovered by Charles Brown for using potassium hydride to prepare potassium ketone enolates[4] together with a report[5] that KH reacts with methyl iodide only sluggishly at 50 °C suggested a simple route. Treatment of cyclohexanone with a fourfold excess of KH and methyl iodide at 25 °C might lead directly to the desired ketone. Indeed, with slight modifications of this procedure, the results were sufficiently gratifying that we applied the method to a variety of ketones and report our results here.

Results and Discussion

Reaction of KH with Methyl Iodide. A suspension of KH (10 mmol) in tetrahydrofuran (THF) was maintained at 25 °C and treated with 10 mmol of methyl iodide. Evolution of a gas determined to be methane (GLC retention volume) began immediately. A total of 3.7 mmol of methane was formed in less than 1 min (as measured by a gas buret). No further methane was formed over a 2-h period. GLC analysis of the THF suspension confirmed the presence of the expected 6.3 mmol of residual methyl iodide. Additions of 10 mmol of cyclohexanone to the suspension resulted in the rapid evolution of 6.3 mmol of hydrogen, confirming the presence of 6.3 mmol of residual KH.

Evidently, KH does reduce methyl iodide at room temperature, but the reaction stops far short of completion. We have no direct evidence on the reason for the incomplete reduction, but the following experiment was particularly revealing.

A suspension of 15 mmol of KH in THF was treated with 5 mmol of 2,2,6-trimethylcyclohexanone. Hydrogen (5.0 mmol) was evolved over a 5-min period. Injection of 5 mmol of methyl iodide did not produce any gas evolution (<0.1 mmol). GLC analysis of a small aliquot of the reaction mixture revealed the presence of 4.9 mmol of 2,2,6,6-tetramethylcyclohexanone. At this point, the suspension was treated with an additional 10 mmol of methyl iodide and 3.6 mmol of methane was immediately formed. Again the presence of residual KH (6.4 mmol) and methyl iodide (6.4 mmol) was established.

Based on these results, we make the following points. The incomplete reduction of methyl iodide by KH is probably not due to inhibition by the product KI since KI is also formed (presumably in a similar state) by reaction of the ketone enolate with methyl iodide.[6] The incomplete reduction is probably not due to a trace amount of an inhibitor in the methyl iodide unless the inhibitor is removed by the ketone enolate. The incomplete reduction is not due to the presence of some 30% of a highly reactive form of KH unless this highly reactive form does not preferentially react with the ketone. Most importantly, from our point of view, the potassium enolate of 2,2,6-trimethylcyclohexanone is remarkably reactive to methyl iodide and this reaction is much faster than the reduction of methyl iodide with KH.

Permethylation of ketones. Based on the above results, our original concept was modified slightly so as to minimize competing reduction of methyl iodide. Cyclohexanone was added to a THF suspension containing 4.3 equiv of KH. Methyl iodide (4.3 equiv) was then added dropwise to the

Table I. Methylation of Ketones with KH and Methyl Iodide at 25 °C

Ketone	Registry no.	Product	Registry no.	Yield[a]
Cyclobutanone	1191-95-3	2,2,4,4-Tetramethylcyclobutanone	4298-75-3	(79)
Cyclopentanone	120-92-3	2,2,5,5-Tetramethylcyclopentanone	4541-35-9	100 (83)
Cyclohexanone	108-94-1	2,2,6,6-Tetramethylcyclohexanone	1195-93-3	96 (81)
Cycloheptanone		2,2,7-Trimethylcycloheptanone	40514-75-8	75
Cycloheptanone[b]	502-42-1	2,2,7,7-Tetramethylcycloheptanone	64342-79-6	62 (50)
Acetone	67-64-1	2,2,4-Trimethyl-3-pentanone	5857-36-3	90
Acetone[b]		2,2,4,4-Tetramethyl-3-pentanone	815-24-7	72 (60)
Acetophenone	98-86-2	2,2-Dimethylpropiophenone	938-16-9	100 (81)
4-Heptanone	123-19-3	3,3,5-Trimethyl-4-heptanone	51220-07-6	86 (66)

[a] GLC yields, isolated yields (distillation) in parentheses. [b] Reaction mixture refluxed for 1 h prior to addition of the final equivalent of methyl iodide.

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reaction mixture. GLC analysis established a 96% yield of 2,2,6,6-tetramethylcyclohexanone.

Using this procedure, cyclobutanone, cyclopentanone, cyclohexanone, and acetophenone are nearly quantitatively permethylated in 15 min at 25 °C (see Table I). 4-Heptanone and cycloheptanone give cleanly the trimethylated product and acetone the pentamethylated product under these conditions. In these latter cases, the reason for incomplete methylation is slow reaction of the penultimate methylated ketone with KH. With acetone and cycloheptanone, refluxing the reaction mixture for 1 h followed by cooling and addition of the final equivalent of methyl iodide gives the permethylated ketones in good yields. However, this latter procedure is ineffective with 4-heptanone. In fact, no hydrogen was evolved when a sample of 3,3,5-trimethyl-4-heptanone was refluxed for 6 h with KH and the starting ketone was recovered quantitatively after addition of methyl iodide.

Reduction of 2,2,6,6-Tetramethylcyclohexanone with KH. When reaction mixtures for the permethylation of cyclohexanone were allowed to stir for periods of an hour or more prior to workup, small amounts of a side product identified as the methyl ether of 2,2,6,6-tetramethylcyclohexanol were detected. Evidently, a slow reduction of the permethylated ketone by KH occurs.[7] This was confirmed by stirring mixtures containing equivalent amounts of KH and 2,2,6,6-tetramethylcyclohexanone at room temperature and analyzing quenched aliquots periodically for 2,2,6,6-tetramethylcyclohexanol. Ten percent of the starting ketone was reduced in 5 h and 50% in 24 h.

Experimental Section

^{1}H-NMR spectra were recorded on a Varian T-60 with Me_4Si internal standard. Infrared spectra were recorded using a Perkin-Elmer 237B grating spectrometer. GLC analyses and preparative chromatography were obtained with a Varian 920 using 6 ft × 0.25 in. stainless steel columns packed with 1.5% OV-101 on Chromosorb GHP. THF was distilled from the sodium ketyl of benzophenone just prior to use. KH was obtained as a mineral oil suspension (Alpha) and used directly. Methyl iodide and all ketones were distilled and stored under an argon atmosphere. Caution: the paper by Brown[6] should be consulted before handling KH.

Reaction of KH with Methyl Iodide. A 50-mL round-bottomed flask equipped with a magnetic stirring bar, septum inlet, and mercury bubbler was flushed with argon and attached to a gas buret. The flask was charged with 1.86 mL (10 mmol) of KH suspension and 10 mL of THF. Methyl iodide (0.6 mL, 10 mmol) was injected. A total of 93 mL (3.7 mmol) of gas was evolved in 1 min. No further gas was evolved in 2 h. GLC analysis (2.5% $AgNO_3$, and 7% paraffin on Al_2O_3) of a sample of the gas indicated the presence of methane. 1-Pentane (10 mmol) was added to the reaction mixture as internal standard and GLC analysis (1.5% OV-101) of an aliquot established the presence of 6.3 mmol of methyl iodide.

Permethylation of Ketones. Because of the volatility of methyl iodide, it was found best to use a dry ice condenser on the reaction flask. The following procedure for the permethylation of cyclohexanone is representative of the general technique. A 500-mL round-bottomed flask was equipped with a magnetic stirring bar, septum inlet, and dry ice condenser and flushed with argon. The flask was charged with 40 mL (216 mmol) of KH in mineral oil. The flask was then immersed in a water bath maintained at 25 °C. THF (220 mL) was injected followed by dropwise addition of cyclohexanone (5.2 mL, 50 mmol) over a 5-min period. After 5 min of additional stirring, methyl iodide (13.5 mL, 216 mmol) is added dropwise over a 15-min period. After an additional 15 min of stirring, the reaction mixture is treated cautiously with 15 mL of water. The aqueous layer is extracted with one 15-mL portion of ether and the combined organic layers are dried over anhydrous K_2CO_3. The organic layer is subjected to simple distillation to obtain 6.25 g, 81% yield, of 2,2,6,6-tetramethylcyclohexanone: bp 183–185 °C; ^{1}H NMR (CCl_4, internal Me_4Si) δ 1.6 (s, 6 H), 1.1 (s, 12 H); IR (neat) 1700 cm^{-1} (C=O). Using this procedure, the following compounds were obtained (all new products gave satisfactory C, H elemental analysis):

2,2,4,4-Tetramethylcyclobutanone: isolated yield, 65%; bp 130–133 °C; ^{1}H NMR (CCl_4, internal Me_4Si) δ 1.7 (s, 2 H), 1.2 (s, 12 H); IR (neat) 1780 cm^{-1} (C=O).

2,2,5,5-Tetramethylcyclopentanone: isolated yield, 83%; bp 153 °C; ^{1}H NMR (CCl_4, internal Me_4Si) δ 1.7 (s, 4 H), 1.0 (s, 12 H); IR (neat) 1745 cm^{-1} (C=O).

2,2,7-Trimethylcycloheptanone: isolated by preparative GLC; ^{1}H NMR (CCl_4, internal Me_4Si) δ 2.6–3.0 (m, 1 H) [1.2–2.0 (m, 8 H), 1.0 (s, 6 H), 0.9 (α, 3 H)]; IR (neat) 1710 cm^{-1} (C=O).

2,2,4-Trimethyl-3-pentanone: isolated by preparative GLC; ^{1}H NMR (CCl_4, internal Me_4Si) δ 3.0 (heptet, 1 H, J = 8 Hz), 1.1 (s, 9 H), 1.0 (d, 6 H, J = 8 Hz); IR (neat) 1705 cm^{-1} (C=O).

2,2-Dimethylpropiophenone: isolated yield, 81%; bp (5 Torr) 85–90 °C; ^{1}H NMR (CCl_4, internal Me_4Si) δ 7.5 (m, 2 H), 7.2 (m, 3 H), 1.3 (s, 9 H); IR (neat) 1675 cm^{-1} (C=O).

3,3,5-Trimethyl-4-heptanone: isolated yield, 66%; bp 187 °C; ^{1}H NMR (CCl_4, internal Me_4Si) δ 2.7 (m, 1 H), 1.4 (m, 4 H), 1.0 (s, 6 H), 1.8 (m, 3 H); IR (neat) 1695 cm^{-1} (C=O).

The following compounds were obtained by a modification of the above procedure by which the reaction mixture was heated to reflux for 1 h after addition of one less than the theoretical equivalent of methyl iodide. The reaction flask was then immersed in a water bath at 25 °C and the final equivalent of methyl iodide was injected dropwise. Workup was as described above.

2,2,7,7-Tetramethylcycloheptanone: isolated yield, 50%; bp 195 °C; ^{1}H NMR (CCl_4, internal Me_4Si) δ 1.6 (s, 8 H), 1.1 (s, 12 H).

2,2,4,4-Tetramethyl-3-pentanone: isolated yield, 60%; bp 157 °C; ^{1}H NMR (CCl_4, internal Me_4Si) δ 1.2 (s); IR (neat) 1670 cm^{-1}.

Acknowledgment is made to the National Science Foundation for partial support of this work.

Registry No.—KH, 7693-26-7; methyl iodide, 74-88-4.

References and Notes

(1) Cf. F. C. Whitmore and E. E. Stahly, *J. Am. Chem. Soc.*, **55**, 4153 (1933).

(2) J. M. Conia, *Bull. Soc. Chim. Fr.*, 537 (1950).

(3) Cf. H. O. House, "Modern Synthetic Reactions", 2nd ed, W. A. Benjamin, Menlo Park, Calif., 1972, pp 546–570.

(4) C. A. Brown, *J. Org. Chem.*, **39**, 1324 (1974).

(5) C. A. Brown, *J. Am. Chem. Soc.*, **95**, 982 (1973).

(6) It is interesting to note that treatment with methyl iodide is recommended for activation of KH which has been exposed to the atmosphere: C. A. Brown, *J. Org. Chem.*, **39**, 3913 (1974).

(7) A similar reduction of nonenolizable ketones by sodium hydride has been described: F. W. Swamer and C. R. Hauser, *J. Am. Chem. Soc.*, **68**, 2647 (1946).

Thiol–Olefin Cooxidation Reaction. 6. A New Convenient Route to 1-Substituted Indenes. Indenone as Dienophile in Diels–Alder Reactions

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A recent publication[1] concerning the use of indenone ketals as dienophiles in a Diels–Alder reaction with butadiene (to give adducts that then serve as starting materials for the synthesis of degradation products of the plant stimulant gibberellic acid) prompts us to report the use of indenone itself in the cycloaddition reaction and its convenient preparation from indene as well as of other 1-substituted indenes (**4–6**). The facile conversion of indene by means of the TOCO reaction to a mixture of three isomeric β-hydroxy sulfoxides[2,3] followed by their oxidation to β-keto sulfoxides[4] was coupled with the ready elimination of the sulfoxide moiety to give the 1-substituted indenes as shown in Scheme I.

The formation of **4** requires refluxing overnight in toluene as compared to a 4-h period of reflux for the formation of **5** and **6**. The longer time required for the elimination of the sulfoxide moiety in the case of the formation of **4** suggests the stabilization of **2** by intra- and intermolecular hydrogen bonding.

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