TABLE I

REACTION OF α,α-DICHLORO-β-KETO ESTERS WITH REPRESENTATIVE BASES[a]

Registry no. (ester)	α,α-Dichloro-β-keto ester	Registry no. (base)	Base	Reaction time, min	Products identified (mmol)
6134-66-3	$MeCOCCl_2COOEt$	7542-12-3	$NaHCO_3$	30	MeCOONa (8)[b]
					$HCCl_2COOEt$ (10)
		127-08-2	$KOCOCH_3$	15	MeCOOEt (10)
					$HCCl_2COOEt$ (10)
		532-32-1	$NaOCOC_6H_5$	15	C_6H_5COOEt (8)
					MeCOOEt (1)
		141-52-6	NaOEt	1	MeCOOEt (9)
					$HCCl_2COOEt$ (10)
		109-89-7	Et_2NH	1	$MeCONEt_2$ (8)
					$HCCl_2COOEt$ (9)
42071-71-6	$C_6H_5COCCl_2COOEt$		$KOCOCH_3$	15	C_6H_5COOEt (8)
					MeCOOEt (1)
					$HCCl_2COOEt$ (9.5)
			NaOEt	1	C_6H_5COOEt (8)
					$HCCl_2COOEt$ (9)
			Et_2NH	1	$C_6H_5CONEt_2$ (8.5)
					$HCCl_2COOEt$ (9.5)

[a] A mixture of α,α-dichloro-β-keto ester (10 mmol), ethanol (10 ml), and the appropriate base (10 mmol) was stirred at 25°. The reaction mixture was then analyzed by glpc (5% DC 550 on Chromosorb W) using an internal standard. [b] Yield by isolation.

The α,α-dichloro-β-keto esters required in the present study were synthesized by the chlorination of the corresponding β-keto esters with sulfuryl chloride.[4] Our improved procedure, described herein, now provides these dichloro keto esters in virtually quantitative yields. The formation of any side products in these chlorinations is negligible (glpc, nmr), thus permitting the direct use of these powerful lacrymators without further purification.

The novel fragmentation reaction reported here demonstrates the potential of readily available α,α-dichloro-β-keto esters as acyl transferring agents. Also, this reaction could be useful in organic structural elucidation where the degradation of a β-keto acid (ester) moiety can now be achieved under very mild conditions to give readily identified fragments of defined functionality.[5]

Experimental Section[6]

Preparation of α,α-Dichloro-β-keto esters.—*Caution:* α,α-Dichloro-β-keto esters are powerful lacrymators. The preparation of these compounds should be conducted in a well-ventilated hood.

The synthesis of ethyl α,α-dichloroacetoacetate is representative of this procedure. Ethyl acetoacetate (6.5 g, 50 mmol) was placed in a round-bottom flask and sulfuryl chloride (14.9 g, 110 mmol) was added to it in 0.5 hr keeping the reaction temperature below 35° with occasional cooling. After the reaction mixture was stirred for an additional 0.5 hr at 25°, glpc analysis showed a quantitative yield of the desired product. The residual sulfuryl chloride was removed under vacuum, and the crude compound thus obtained (98% pure) was used in the subsequent reactions: nmr ($CDCl_3$, TMS) δ 1.33 (t, 3 H, J = 7 Hz), 2.80 (s, 3 H), and 4.39 (q, 2 H, J = 7 Hz).

Ethyl α,α-dichlorobenzoylacetate was prepared by a similar procedure in 98% yield: nmr ($CDCl_3$, TMS) δ 1.15 (t, 3 H, J = 7 Hz), 4.31 (q, 2 H, J = 7 Hz), 7.56, and 7.96 (m, 5 H).

Reaction of α,α-Dichloro-β-keto Esters with Bases.—A typical reaction is described here. To a stirred mixture of potassium acetate (22.1 g, 225 mmol) and ethanol (90 ml), ethyl α,α-dichloroacetoacetate (43.0 g, 225 mmol) was added in 0.5 hr. The reaction was slightly exothermic (25° → 35°), and, after an additional 15 min, glpc analysis showed it to be complete. The composition of the reaction mixture was determined (Table I), and then water (400 ml) was added to it. After extraction with methylene chloride and drying, distillation gave 32.6 g (92%) of ethyl dichloroacetate: bp 152–156°; nmr ($CDCl_3$, TMS) δ 1.33 (t, 3 H, J = 7 Hz), 4.32 (q, 2 H, J = 7 Hz), and 5.95 (s, 1 H).

The reactions with other bases were performed in an identical manner.

Reaction of Ethyl α,α-Dichloroacetoacetate with a Catalytic Quantity of Potassium Acetate.—This experiment was performed according to the general procedure described above, except that only 5 mol % of potassium acetate per mole of dichloro ester was used. The reaction required 30 min for completion at 35°.

Reaction of Ethyl α,α-Dichloroacetoacetate with Potassium Acetate in Benzene.—A mixture of ethyl α,α-dichloroacetoacetate (4.98 g, 25 mmol), potassium acetate (2.45 g, 25 mmol), and benzene (25 ml) was stirred at 25° for 12 hr. Ir and glpc analysis of the benzene solution revealed the absence of any acetic anhydride. Upon the addition of ethanol (5 ml) to this reaction mixture, a rapid reaction occurred giving ethyl acetate (24 mmol) and ethyl dichloroacetate (24 mmol).

Acknowledgments.—The author wishes to thank Dr. R. K. Blackwood for stimulating discussions and Mr. H. J. Slater for expert technical assistance.

(4) D. P. Wyman, P. R. Kaufman, and W. R. Freeman, *J. Org. Chem.*, **29**, 2706 (1964). For a recent discussion on the mechanism of ketone halogenation, see K. E. Teo and W. W. Warnhoff, *J. Amer. Chem. Soc.*, **95**, 2728 (1973).

(5) For a recent application of this concept in the structural determination of certain α,α-dihalocyclobutanones, see L. Ghosez, R. Montaigne, A. Roussel, H. Vanlierde, and P. Mollet, *Tetrahedron*, **27**, 615 (1971).

(6) Melting points were taken on a Fisher-Johns apparatus and are uncorrected. Glpc analyses were performed on a DC-550, 5% on Chromosorb W, 5 ft × 0.25 in. column. Nmr spectra were recorded on a Varian A-60 instrument.

Lithiotriphenylphosphinioacetonide as a Convenient Reagent for the Introduction of the Acetonyl Synthon

MANNING P. COOKE, JR.

Department of Chemistry, Washington State University, Pullman, Washington 99163

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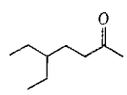
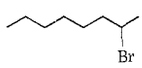
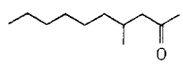
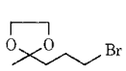
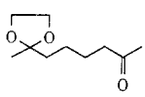
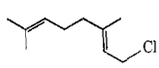
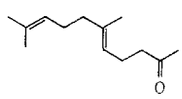
We wish to report that lithiotriphenylphosphinioacetonide (2) prepared from readily available acetyl-

TABLE I

PREPARATION OF KETONES FROM ALKYL HALIDES

Entry	Registry no. (alkyl halide)	Alkyl halide	Reaction scale, mmol RX[a]	Phosphorane hydrolysis time, hr[b]	Registry no. (ketone)	Ketone	Isolated yield, %
1	100-44-7	$PhCH_2Cl$	100	40[c]	2550-26-7	$PhCH_2CH_2\overset{O}{\overset{\|}{C}}CH_3$	76[d,e]
2	110-53-2	$CH_3(CH_2)_3CH_2Br$	100	8[f]	111-13-7	$CH_3(CH_2)_4CH_2\overset{O}{\overset{\|}{C}}CH_3$	82
3	693-58-3	$CH_3(CH_2)_7CH_2Br$	100	22	6175-49-1	$CH_3(CH_2)_3CH_2\overset{O}{\overset{\|}{C}}CH_3$	93
4	3814-34-4		79	12	40238-93-5		78
5	557-35-7		68[g]	18	42071-54-5		39
6	24400-75-7		66	24	26118-50-3		58[h]
7	4490-10-2		40	12	689-67-8		85

[a] Typical runs (see Experimental Section) used a ratio of ylide:BuLi:RX of 1.08:1.05:1.00 with a reaction time of approximately 1 hr at 0° for the alkylation step. [b] Hydrolyses were conducted by heating a solution of crude phosphorane **3** in EtOH–H_2O at 75–85°. The pH of these solutions was 8–10 owing to the slight excess of ylide anion **2** employed in the alkylation step. [c] Reduction of the hydrolysis time to 8 hr resulted in a 44% yield of ketone. [d] A yield of 92% (glpc) was obtained on a 1-mmol scale. [e] The intermediate phosphorane **3** was isolated in 97% yield. [f] A yield of 71% (glpc) was obtained when the hydrolysis was conducted for 20 hr after the solution was adjusted to pH 7 by the addition of HOAc. [g] The alkylation reaction was conducted at 0° for 3 hr followed by 12 hr at 25° followed by 50° for 1 hr. [h] New compound, bp 110–112° (3 mm). *Anal.* Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.78; H, 9.75.

methylenetriphenylphosphorane[1] (**1**) is a convenient reagent for the introduction of the acetonyl group by nucleophilic displacements on alkyl halides. Analogous to the formation of dianions from enolates,[2] we and others[3] have found that treatment of **1** with strong bases such as lithium diisopropylamide or butyllithium in THF at −78° gives rise to the stable, highly colored ylide anion **2**. Ylide anion **2** is highly nucleophilic and is alkylated by a variety of alkyl halides to give the substituted β-ketophosphorane **3** in high yield.[5] That

$$\underset{\mathbf{1}}{CH_3\overset{O}{\overset{\|}{C}}CH{=}PPh_3} \qquad \underset{\mathbf{2}}{LiCH_2\overset{O}{\overset{\|}{C}}CH{=}PPh_3} \qquad \underset{\mathbf{3}}{RCH_2\overset{O}{\overset{\|}{C}}CH{=}PPh_3}$$

the anion is efficiently formed and readily alkylated is illustrated by the treatment of **1** with butyllithium at −78° for 15 min in THF followed by alkylation with benzyl chloride at 0° (20 min) giving after work-up the substituted phosphorane **3**[6] (R = benzyl) in 97% isolated yield. Most significantly we have found that **2** is efficiently alkylated by ordinary alkyl bromides.[5] Completion of the alkylation reaction is conveniently signaled by the disappearance of the intense color of **2**.

While the newly formed phosphoranes are useful in Wittig-type olefination reactions[4,7] we have found that the simple hydrolysis[1] of these acylphosphoranes in combination with the facile alkylation of ylide anion **2** allows a mild, high-yield method for the introduction by nucleophilic substitution of the acetonyl synthon in the manner classically accomplished by the acetoacetic ester synthesis. Examples are shown in Table I. While alkylations of acetoacetic ester salts often proceed slowly and in moderate yields with other than active halides,[8] alkylations of ylide anion **2** proceed rapidly at 0° with no evidence of other than monoalkylation of **2**, and isolation of the intermediate **3** is not required. In addition, completion of the ketone

$$\mathbf{2} \xrightarrow{RX} \mathbf{3} \xrightarrow{H_2O} RCH_2\overset{O}{\overset{\|}{C}}CH_3 + Ph_3PO$$

(1) F. Ramirez and S. Dershowitz, *J. Org. Chem.*, **22**, 41 (1957).

(2) T. M. Harris and C. M. Harris in "Organic Reactions," Vol. 17, W. G. Dauben, Ed., Wiley, New York, N. Y., 1969, Chapter 2.

(3) After the completion of this work there appeared a report describing the preparation of this anion in a similar manner and the use of subsequently prepared substituted phosphoranes in Wittig-type olefination reactions (ref 4.

(4) J. D. Taylor and J. F. Wolf, *Chem. Commun.*, 876 (1972).

(5) Taylor and Wolf[4] have reported that **2** is alkylated at low temperatures by active halides such as benzyl bromide and allyl bromide and by a single alkyl halide, butyl iodide, to give substituted acylphosphoranes in moderate yields.

(6) H. J. Bestmann and B. Arnason, *Chem. Ber.*, **95**, 1513 (1962).

(7) A. Maercker in "Organic Reactions," Vol. 14, R. Adams, Ed., Wiley, New York, N. Y., 1965, p 270.

(8) H. O. House, "Modern Synthetic Reactions," 2nd ed, W. A. Benjamin, Menlo Park, Calif., 1972, pp 510–546.

synthesis *via* the acetoacetic ester method often requires removal of the carboalkoxy control group under conditions requiring either high and low pH or hydrogenolysis of special esters if these conditions are to be avoided,[8] while the hydrolysis of **3** is accomplished by heating with ethanol–water under neutral or slightly basic conditions. As seen in Table I, halides containing groups threatened by acidic conditions (entries 6 and 7) are readily converted to the corresponding acetone derivative. Secondary bromides are less satisfactory for this process, however, presumably owing to their increased susceptibility to E2 elimination under the influence of highly basic nucleophiles.[9]

Experimental Section

n-Butyllithium was obtained from Matheson Coleman and Bell as a 1.6 *N* solution in hexane. Reagent grade tetrahydrofuran was distilled from $LiAlH_4$ immediately prior to use for small-scale reactions but used without purification for large-scale reactions. Starting materials were obtained from commercial sources or prepared by literature procedures. Alkyl bromides were distilled prior to use. All products were characterized by spectral and glpc comparison with authentic samples when available and through the melting points of their semicarbazone derivatives. New compounds gave satisfactory elemental analyses which were performed by the Analytical Laboratory of the University of Idaho.

The following experimental procedure is representative of the method developed for the preparation of methyl ketones from alkyl halides. Any variations in conditions are given in Table I.

2-Dodecanone from 1-Bromononane.—In 800 ml of dry THF under a nitrogen atmosphere was placed 34.4 g (0.108 mol) of acetylmethylenetriphenylphosphorane[1] (**1**). The solution was cooled by means of a Dry Ice–acetone bath and with stirring there was added 67 ml of 1.6 *N* butyllithium in hexane (0.105 mol) beyond the point where the red color of the ylide anion persisted. The intensely colored solution was stirred at −78° for 15 min, whereupon 20.7 g (0.100 mol) of 1-bromononane was added and the Dry Ice bath was replaced by an ice–water bath. The solution was stirred at 0° for 1 hr, whereupon the color of the ylide anion was nearly discharged. The solvent was removed under reduced pressure and the residue was dissolved in 300 ml of ethanol followed by the addition of water approaching the cloud point (approximately 200 ml). The resulting solution was heated (steam bath) for 22 hr and then poured into brine solution and extracted with two portions of pentane. Distillation of the oil obtained after removal of the solvent gave 17.1 g (93%) of 2-dodecanone, bp 77–78° (0.6 mm) [lit.[10] bp 120° (12 mm)].

The following procedure illustrates the preparation and isolation of the intermediate substituted phosphorane **3** obtained by alkylation of **2**.

3-Phenylpropionylmethylenetriphenylphosphine (3, R = Benzyl).—A solution containing 3.18 g (10.0 mmol) of **1** in 100 ml of THF was treated with 10.5 mmol of *n*-butyllithium at −78° as described above. The resulting solution containing anion **2** was then treated with 1.33 g (10.5 mmol) of benzyl chloride and the resulting mixture was stirred at 0° for 20 min. The mixture was warmed to room temperature whereupon the color of **2** was discharged. The reaction mixture was poured into an ice–water mixture with vigorous stirring and the product, 3.94 g (97%), was collected by filtration. Recrystallization from ethyl acetate gave 3.30 g (82%) of pure **3** (R = benzyl), mp 150–152° (lit.[6] mp 148–150°).

Acknowledgment.—We thank the Research Corporation and Washington State University for their supports through grants-in-aid.

Registry No.—**1**, 1439-36-7; **2**, 38938-34-0.

(9) J. Hine, "Physical Organic Chemistry," McGraw-Hill, New York, N. Y., 1956, p 180.

(10) T. Shenton and J. C. Smith, *Chem. Ind. (London)*, 1510 (1958).

Stereoselectivity in the Base-Catalyzed Decarboxylation of 5,5-Dicarboxy-2-isopropyl-1,3-dioxane

HAROLD D. BANKS

Department of Chemistry, University of Bridgeport, Bridgeport, Connecticut 06602

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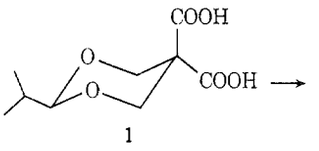
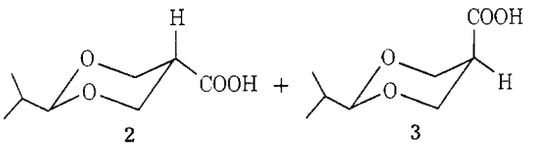
Some years ago Zimmerman and Giallombardo studied the stereochemical consequences of base-catalyzed decarboxylation of 4-phenylcyclohexane-1,1-dicarboxylic acid.[1] They found that *cis*-4-phenylcyclohexanecarboxylic acid comprises 57% of the product regardless of whether the solvent is 2,4,6-trimethylpyridine or nonbasic 1,3,5-trimethylbenzene. In striking contrast to these results, the product composition in the decarboxylation of solutions of 5,5-dicarboxy-2-isopropyl-1,3-dioxane (**1**) in pyridine and aniline derivatives depends critically on the solvent.



1



2 3

Solutions of **1** (0.1–0.2 *M*) dissolved in the desired pyridine or aniline base were decarboxylated at constant temperature. The predominant product was **2** with every base except 2,6-dimethylpyridine. The results are given in Table I.

TABLE I

PRODUCT COMPOSITION IN THE DECARBOXYLATION OF 5,5-DICARBOXY-2-ISOPROPYL-1,3-DIOXANE

Solvent	% 3 at 100.0°	% 3 at 125.0°
Pyridine	41.4 ± 0.1	
2-Methylpyridine	35.9	
2,6-Dimethylpyridine	56.3	56.3 ± 0.1
3,5-Dimethylpyridine	33.4	33.3
Aniline	24.2	27.5
N-Methylaniline	16.9	
N,*N*-Dimethylaniline	11.7	17.6

One possible mechanism for this reaction is the concerted loss of carbon dioxide and protonation, occurring with either retention or inversion of configuration. The product composition is determined by which carboxyl group departs. To test this mechanism, the kinetics of the reaction were studied using four bases at 100.0, 110.0, and 125.0°. The rate constants were all pseudo first order, and are given in Table II. If the composition of the product is determined exclusively by which diastereotopic carboxyl group is displaced, the product composition may be used to partition each rate constant into a rate constant for loss of

(1) H. E. Zimmerman and H. J. Giallombardo, *J. Amer. Chem. Soc.*, **78**, 6259 (1956).