For comparing the stability of DMPOC and carbobenzoxy (Z) groups in catalytic hydrogenolysis, the protected dipeptide Z–MetGlyOEt[4] was synthesized and subjected to catalytic hydrogenolysis under the same conditions used in the deblocking of III. A quantitative recovery of starting material was thus obtained.

The DMPOC group was also hydrogenolyzed from S-protected cysteine peptides. Accordingly, DMPOC S-benzyl cysteine was coupled via carbodiimide to glycine-L-phenylalanine methyl ester hydrochloride to give the DMPOC tripeptide VIII Hydrogenolysis of VIII in methanol over 0.5 g of palladized carbon (5%)/ mmol gave the tripeptide IX in 51% yield as the hydrochloride

In summary, the success of catalytic hydrogenolysis of the DMPOC protecting group in the presence of sulfur-containing peptides makes DMPOC useful as a protecting group for general peptide synthesis The application of the DMPOC group and other tertiary acetylenic urethane-protecting groups to the synthesis of known biologically active sulfur-containing peptides is currently under investigation.

Acknowledgment. We are grateful to Dr. E. H. Flynn for his encouragement and helpful discussions.

(4) Yield 54%; mp 91–92°. Anal. Calcd for $C_{17}H_{42}N_2O_5S$: C, 55.42; H, 6.57; N, 7.60; O, 21.70; S, 8.70. Found: C, 55.64; H, 6.54; N, 7.48; O, 21.63; S, 8.69.
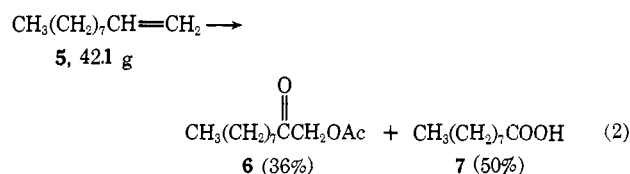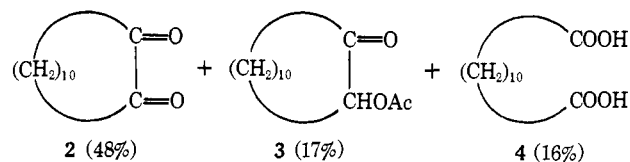
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Permanganate in Acetic Anhydride. α-Diketones Directly from Olefins

Sir:

We have found that potassium permanganate in acetic anhydride effects the following unique conversions[1] (eq 1 and 2). Further examples of oxidations

(1)

$$CH_3(CH_2)_7CH=CH_2 \longrightarrow$$

5, 42.1 g

$$CH_3(CH_2)_7\overset{O}{\overset{\|}{C}}CH_2OAc + CH_3(CH_2)_7COOH \quad (2)$$

6 (36%)   7 (50%)

by this new reagent are illustrated in Table I.

Although reaction 1 should now become the method of choice for preparing α-diketones from acyclic or

(1) The yields indicated are for isolated pure substances.

Table I. Oxidations by Potassium Permanganate in Acetic Anhydride[a]

| Starting material | —Yields, %— | | % DME[b] | Reaction time, hr | Mole equiv of MnO₄⁻ |
	α-Diketone	Keto acetate			
trans-Cyclododecene[c,f]	68	10	0	2	4
	50	5	50	3	4
cis-Cyclododecene[d]	20	1	0	2	4
α-Hydroxycyclododecanone (8)[e]	69	4	25	3	4
trans-5-Decene[f]	66	15	0	3	3
cis-5-Decene[f]	42	9	0	3	3
trans-Stilbene[g]	46	15	25	3	4
cis-Stilbene[g]	60	12	0	3	4
	50	13	25	3	4
Benzoin (9)	73	12	25	3	4
Oleic acid	42		0	1	4
1-Decene		40	0	5	3
Styrene		33	0	1	3

[a] In each experiment the pulverized permanganate was added in one batch to a stirred solution of 6 mmol of starting material in 40 ml of acetic anhydride cooled in an ice bath. Each reaction was stirred in the ice bath for the indicated time; work-ups were performed as described for the large scale reaction of olefin **1**. Yields were determined by glc and/or uv analysis. In the cases of 1-decene and styrene, 2 g of anhydrous potassium acetate was added before the permanganate. [b] The total reaction volume was always 40 ml but in some cases as much as 50% of the acetic anhydride was replaced by dimethoxyethane (DME). [c] This material was only 91% trans-cyclododecene (see ref 2). [d] M. Ohno and M. Okamoto, *Org. Syn.*, **49**, 30 (1969). [e] Prepared from the epoxide by the procedure of T. Cohen and T. Tsuji, *J. Org. Chem.*, **26**, 1681 (1961). [f] Obtained from Chemical Samples Co. [g] Benzoin was also produced in ca. 20% yield. This contrasts with the oxidations of the cyclododecenes and of the 5-decenes where the α-hydroxy ketones are very minor products.

large ring disubstituted olefins, it fails to produce significant amounts of α-diketones from smaller ring olefins such as cyclohexene and norbornene.[1a] It appears that reaction 1 will succeed only when the carbonyls of the desired α-diketone are not constrained to a cisoid orientation.

The following procedure for the conversion of cyclododecene (**1**) to the dione **2** illustrates how the reaction is performed on a large scale. A 6-l. erlenmeyer flask with a 3 in. × ¹/₂ in. magnetic stirring bar was charged with 2 l. of acetic anhydride and 50 g (0.30 mol) of cyclododecene.[2] The resulting solution was cooled to 5° by stirring[3] in a large ice–salt bath and 190 g (1.2 mol) of potassium permanganate[4] was added in four portions over a period of 30 min; an exothermic reaction occurs. The permanganate should be added more slowly if necessary to prevent the temperature of the reaction mixture from exceeding 10°. After completion of the addition the mixture was stirred in the cooling bath for 90 min (temperature at this point, 6°). Ice cold hexane–ethyl acetate (1:1; 2 l.) was added, followed by 2 l. of an ice–water (0°) solution containing 250 g of sodium bisulfite. After stirring in the cooling bath for several minutes the mixture was transferred to a 6-l. separatory funnel and the

(1a) NOTE ADDED IN PROOF. cis-Cyclooctene, the smallest cyclic olefin to be successfully oxidized, gave a 23% yield of diketone.

(2) Eastman Kodak 99+% acetic anhydride was used as obtained. The cyclododecene was purchased from Chemical Samples Co.; glc analysis revealed 91% trans, 7% cis, and 2% diene.

(3) Efficient stirring was ensured by use of the powerful "9 × 9" Cole Palmer magnetic stirrer.

(4) Fisher reagent grade permanganate was pulverized in a mortar prior to addition.

aqueous phase was drawn off.[5] The organic layer was washed numerous times with water and finally 1 N NaOH to remove most of the acetic anhydride. The solvent and most of the remaining acetic anhydride were removed on a rotary evaporator.

The resulting deep yellow oil was dissolved in 200 ml of pyridine and 100 ml of water was dropped in slowly while stirring in an ice bath.[6] After stirring for 10 min at room temperature, hexane–ethyl acetate (1:1) and water were introduced. The organic layer was separated and after washing with base, acid, and water, it was dried over magnesium sulfate and concentrated to give 41.2 g of a yellow solid. At this point the only contaminants remaining were the keto acetate 3 and a small amount of starting olefin 1. Distillation afforded 27.9 g (48% yield) of dione 2, bp 83–85° (0.1 mm), mp 42.5–43.5°;[7] the pot contained 12.3 g of essentially pure keto acetate 3. Using methanolic potassium hydroxide the keto acetate was hydrolyzed to the α-hydroxy ketone which in the same reaction vessel, following the procedure of Blomquist and Goldstein,[8] was oxidized by cupric acetate to dione 2 in 90% yield (9.1 g) This raised the total isolated yield of α-diketone 2 to 37.0 g (63%).

Reaction 2 was also performed on a large scale and 42.1 g (0.300 mol) of 1-decene (5) was transformed to 22.7 g (36% isolated yield) of keto acetate 6, mp 49–55°.[9] With the following exceptions the procedure was identical with that described for oxidation of 1: 108 g of anhydrous potassium acetate[10] was added to the reaction mixture before permanganate addition; after permanganate addition, stirring was continued in the ice–salt bath for 5 hr.

The mechanism of these new transformations is currently under study and will be the subject of a later publication. However, we wish to point out several observations which bear on the synthetic utility of the reagent. Ketols 8 and 9 are readily oxidized by the $MnO_4^- $–$Ac_2O$ reagent to the corresponding α-diketones. With the exception of the stilbenes, trans isomers are converted more efficiently to diketone than the cis isomers. This trend is especially apparent with the cyclododecenes where the yield of diketone from the trans isomer is greater than three times that from the cis isomer under identical conditions. When reaction 1 was quenched hydrolytically at an early stage (ca. $^1/_2$ hr) the α-hydroxy ketone 8 was present in amounts comparable to those of diketone 2 and keto acetate 3. We found that under the standard reaction conditions

primary alcohols are acetylated much faster than they are oxidized and are thus automatically protected, whereas with secondary alcohols the rate of oxidation to the ketone is comparable to the rate of acetylation.

Although the permanganate ion exhibits unique reactivity toward olefins, its usefulness in organic synthesis has been severely limited by solubility problems. Solubility is of less concern with the $MnO_4^- $–$Ac_2O$ reagent since most organic substrates are soluble in acetic anhydride. However, some molecules, especially crystalline ones, are not soluble in acetic anhydride at the lower temperatures employed; in such cases (e.g., trans-stilbene and ketols 8 and 9) one can use dimethoxyethane (DME) as a diluent. A solution of the substrate in DME is added to the acetic anhydride. We found that one can replace as much as 50% of the acetic anhydride by DME without major decreases in the yield of diketone (Table I).

α-Diketones are valued as precursors of transition metal ligands, of acetylenes, and of heterocyclic compounds. Our new α-diketone synthesis makes this hitherto rare functional group much more readily accessible.

Caution! When working with more than 100 ml of acetic anhydride the instructions for cooling during the extraction must be heeded.[5]

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Peroxy Acid Oxidation of Phosphinothioates, a Reversal of Stereochemistry

Sir:

We wish to report that thiophosphoryl (P=S) compounds are rapidly, quantitatively, and stereospecifically converted to phosphoryl (P=O) compounds by organic peroxy acids under mild conditions. More strikingly, the stereochemistry at phosphorus can be either retained or inverted depending on the acidity of the system.

Several direct oxidations of thiophosphoryl groups have been reported, usually under vigorous conditions.[1] Despite the similarity of this conversion to the Wittig reaction of phosphorus ylides, little data on the mechanism or stereochemistry of this oxidation are available.[2-4]

(5) The extraction should be carried out quickly and the aqueous acetic anhydride phase should be washed down the sink; after warming to a certain point this layer hydrolyzes violently. In fact, if the extracting solvent and the bisulfite solution are not cooled to 0° vigorous hydrolysis may begin before the aqueous phase can be separated. This happened in an early experiment and the organic phase boiled right out of the separatory funnel. We have not had another accident of this type, since the cooling procedures now employed provide a good margin of safety. By contrast the smaller scale reactions (Table I) involving 30–60 ml of acetic anhydride never got out of control during the extraction even when room temperature water and extraction solvent were used.

(6) This serves to hydrolyze any remaining acetic anhydride as well as the mixed anhydrides of the diacid 4.

(7) Lit. bp 99–101° (1.5 mm), mp 43°: C. W. N. Cumper, G. B. Leton, and A. I. Vogel, *J. Chem. Soc.*, 2067 (1965).

(8) A. T. Blomquist and A. Goldstein, "Organic Syntheses," Collect. Vol. 4, Wiley, New York, N. Y., 1963, p 838.

(9) Lit. mp 55°: K. L. Rinehart, C. L. Tarimu, and T. P. Culbertson, *J. Amer. Chem. Soc.*, 81, 5007 (1959).

(10) Anhydrous potassium acetate was found to have a beneficial effect on the yield of keto acetate from 1-alkenes.

(1) For summaries, see L. Maier, *Top. Phosphorus Chem.*, 2, 43 (1965); K. Sasse, "Methoden der Organischen Chemie," (Houben-Weyl), Vol. XII/1, Georg Thieme Verlag, Stuttgart, 1963; Vol. XII/2, 1964.

(2) L. Horner and H. Winkler (*Tetrahedron Lett.*, 175 (1964)) reported predominant retention on oxidation of a phosphine sulfide with permanganate in pyridine–water.

(3) S. Trippett, Heteroatom Symposium, London, Ontario, 1970, reported oxidation of O-methyl tert-butylphenylphosphinothioate with hydrogen peroxide in refluxing ethanol in which optical activity was maintained; the stereochemistry was not assigned.

(4) J. Michalski, A. Okruszek, and W. Stec (*Chem. Commun.*, 1495 (1970)) recently reported oxidation of an O,O-dialkylphosphonothioate and a phosphine sulfide with nitric acid and with dinitrogen tetroxide. Assuming that optical rotations at 578 and 589 nm are proportional, the