Anal. Calcd. for $C_{10}H_6O_8{\cdot}2H_2O$: H_2O, 12.42. Found: H_2O, 12.40. Calcd. for $C_{10}H_6O_8$: Neut. eq., 63.5. Found: Neut. eq., 63.8.

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New Synthesis of α-Keto Esters

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The importance of α-keto acids and their derivatives as vital biochemical intermediates[2] makes a direct and efficient synthesis of these compounds particularly desirable. We have accomplished this objective by making use of the remarkable ability of selenium dioxide to oxidize active methylene groups.[3,4]

We have found that the reaction of selenium dioxide with an α-bromo ketone of the type $RCOCH_2Br$ in an anhydrous alcohol as solvent produces the corresponding α-keto ester in high yield. From α-bromoacetophenone in absolute ethanol a 70% yield of ethyl benzoylformate was obtained. When methanol was employed as the solvent, the methyl ester was formed in 80% yield.

The reaction path probably involves conversion of the α-halomethyl group to an acid bromide. This would then react rapidly with the solvent to produce the keto ester. The mechanism of the oxidation step is probably the same as that recently postulated by Corey and Schaefer[5] for the reaction of selenium dioxide with a ketone of the type $RCOCH_2R$ to produce an α-diketone.

EXPERIMENTAL

Ethyl benzoylformate. To 9.0 grams (0.074 mol.) of selenium dioxide dissolved in 75 ml. of boiling absolute ethanol was added 15.0 g. of α-bromoacetophenone; the resulting solution was refluxed for 12 hr. The extracts were then poured into water, extracted with ether, dried over magnesium sulfate, and distilled to give 9.2 g. (70% yield) of the desired ester, b.p.$_2$ 97–98°.[6]

Methyl benzoylformate. The same procedure was used to form the methyl ester with the exception that methanol was used as the solvent. The yield was 80%, b.p.$_{14}$ 137°.[7]

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Simplified Zinc-Copper Couple for Use in Preparing Cyclopropanes from Methylene Iodide and Olefins

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It has been recently found that olefins react with methylene iodide and zinc-copper couple to give cyclopropanes.[1] This elegant reaction is quite general in that it is applicable to olefins which are hindered and are either electronegatively- or electropositively-substituted. The method for preparing the zinc-copper couple is important with respect to its reactivity with methylene iodide and its reproducibility for preparing cyclopropanes. The zinc (90%)-copper (10%) couple which has been used most effectively previously is prepared by reaction of zinc dust, cupric oxide, and hydrogen at 500°[1,2] and is subsequently activated by iodine. For purposes of synthesis, this method of obtaining the couple is inconvenient; the activity of the couple is also affected by the temperature at which it is prepared. Couples derived from granulated zinc and copper powder do give cyclopropanes but in erratic yields; those obtained by thermal decomposition of cupric citrate in the presence of zinc dust react with methylene iodide with difficulty.[1]

We would like to report a simple zinc-copper couple which is satisfactory for effecting reaction of methylene iodide with olefins to give cyclopropanes. The couple is prepared simply and rapidly by successive washing of zinc powder with hydrochloric acid (3%), aqueous copper sulfate (2%), water, ethanol, and ethyl ether, respectively.[3] The results obtained for reaction of methylene iodide and the zinc-copper couple in ethyl ether with 1-octene, cyclohexene, (+)-limonene and dihydropyran are

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(1) (a) H. E. Simmons and R. D. Smith, *J. Am. Chem. Soc.*, **80**, 5323 (1958). (b) H. E. Simmons and R. D. Smith, *J. Am. Chem. Soc.*, **81**, 4256 (1959). (c) The present authors should like to acknowledge the private communications of the previous investigators concerning the scope and details of their experimental studies.

(2) F. L. Howard, *J. Research Natl. Bur. Standards*, **24**, 677 (1940); F. R. Buck, B. B. Elsner, E. J. Forbes, S. H. Morrell, J. C. Smith, and E. R. Wallsgrove, *J. Inst. Petroleum*, **34**, 339 (1948).

(3) The method of preparing the zinc-copper couple is essentially that of G. F. Hennion and J. J. Sheehan, *J. Am. Chem. Soc.*, **71**, 1964 (1949).

TABLE I

REACTIONS OF OLEFINS WITH METHYLENE IODIDE/ZINC-COPPER COUPLE

Olefin	Olefin (mol.)	CH_2I_2 (mol.)	Zn(Cu) (mol.)	Reaction Time (hr.)	Product	Yield, %
1-Octene[a]	0.40	0.20	0.30	19	*n*-hexylcyclopropane[b]	55[c,d]
1-Octene[a]	0.40	0.20	0.30	67	*n*-hexylcyclopropane[b]	50[c]
1-Octene[e]	0.40	0.20	0.25	30	*n*-hexylcyclopropane[b]	48[c]
1-Octene[a]	0.40	0.25	0.20	48	*n*-hexylcylcopropane[b]	47[c]
1-Octene[a]	0.40	0.20	0.50	41	*n*-hexylcyclopropane[b]	38[c]
Cyclohexene[a]	0.30	0.15	0.22	67	bicyclo [4.1.0]-heptane[f]	50[c,d]
Cyclohexene[a]	0.40	0.20	0.30	64	bicyclo [4.1.0]-heptane[f]	47[c]
(+)-Limonene[a]	0.15	0.30	0.33	70	1-methyl-4-(1-methylcyclopropyl)cyclohexene[g]	51[d]
Dihydropyran[e,h]	0.15	0.25	0.33	20	2-oxabicyclo[4.1.0] heptane[e]	66[c]

[a] Reaction was effected by adding a mixture of olefin, methylene iodide, and ether to zinc-copper couple. [b] B.p. 148–150°, n_D^{25} 1.4173; lit.[1] b.p. 148°, n_D^{25} 1.4160. [c] Yield computed by gas chromatographic methods. [d] The reaction product was rectified. [e] Reaction was effected by first initiating reaction of zinc-copper couple, methylene iodide, and iodine (0.0006 mol) in ether and then adding the olefin in ether. [f] B.p. 116°, n_D^{25} 1.4542; lit.[1] b.p. 116.5°, n_D^{25} 1.4546. [g] B.p. 69.5–70.2° (8 mm.), n_D^{25} 1.4687; lit.[1] b.p. 73° (8.5 mm.), n_D^{25} 1.4679. [h] The reaction mixture was filtered, washed with excess ammonium hydroxide and then with water until neutral, dried, and distilled.

summarized in Table I. The couple may be prepared in large quantity and compares favorably in general for purposes of synthesis with that obtained by the more elaborate methods. The couple is sufficiently active that it will usually react in ether upon addition of the mixture of olefin and methylene iodide. Reaction could not be initiated in this manner with dihydropyran and methylene iodide. The addition could be executed satisfactorily however by first heating an ether solution of methylene iodide and zinc-copper couple in the presence of iodine and then adding a mixture of dihydropyran in ether. The latter technique has been used successfully with the other olefins and is recommended for use in the Simmons-Smith reaction.

EXPERIMENTAL

Preparation of the zinc-copper couple. Zinc powder (32.8 g., 0.5 mol., Mallinckrodt Analytical Reagent) was washed successively with hydrochloric acid (3%, 4 × 25 ml.), distilled water (4 × 30 ml.), aqueous copper sulfate (2%, 2 × 50 ml.), distilled water (4 × 30 ml.), absolute ethanol (4 × 30 ml.) and absolute ether (5 × 25 ml.).[4] The couple was finally transferred to a Buchner funnel, washed with additional anhydrous ether, covered tightly with a rubber dam, and suction-dried until it reached room temperature. The zinc-copper couple is ready for immediate use in preparation of cyclopropanes.

n-Hexylcyclopropane. A typical procedure for preparing *n*-hexylcyclopropane from 1-octene is described (see Table I). This procedure has also been adapted to the synthesis of the other cyclopropanes of the present study.

Methylene iodide (53.6 g., 0.20 mol.) and iodine (0.15 g., 0.0006 mol.) were added to a mixture of zinc-copper couple (16.3 g. of zinc, 0.25 mol.) and anhydrous ether (165 ml.) in a flask equipped with a stirrer and an efficient water condenser fitted with a calcium chloride tube. The iodine color disappeared immediately; the initial gray-colored mixture was then refluxed for 30 min.[5] During this period the mixture turned darker; the color change was accompanied by a gentle exothermic reaction. External heating was discontinued and 1-octene (44.8 g., 0.4 mol.) in anhydrous ether (25 ml.) was added dropwise in 30 min. During the addition the mixture continued to reflux. Heating was resumed and the mixture refluxed for 30 hr.[6] The reaction mixture was cooled and filtered through a Super Cel pad on a Buchner funnel. The residue was washed thoroughly with ether. The ether solution was extracted with hydrochloric acid (5%, 3 × 50 ml.; to remove dissolved zinc iodide), aqueous sodium bicarbonate (3 × 50 ml.), and saturated aqueous sodium chloride. The aqueous washings were washed with ether; the combined ether extract was filtered through anhydrous magnesium sulfate. After the ether had been removed through a packed column, a mixture (47.7 g.) of 1-octene and *n*-hexylcyclopropane remained.[7] Analysis by gas-phase chromatography (40% polyethylene glycol column, 50°; carrier gas, nitrogen, 17 cm. pressure) revealed that *n*-hexylcyclopropane was obtained in 48% yield. Rectification of an aliquot of the reaction mixture in a Nester spinning band column allowed separation of *n*-hexylcyclopropane in ~50% yield, b.p. 148–150°, n_D^{25} 1.4173, infrared absorption for a cyclopropane ring at 9.88μ, no absorption for an olefin at 6.08μ: lit.[1] b.p. 148°, n_D^{25} 1.4160.

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(4) The washings were performed conveniently by stirring a mixture of the zinc powder and each wash solution with a porcelain spatula in an open beaker and then decanting the supernatant liquid. (b) The washings with hydrochloric acid should be done rapidly to avoid adsorption of bubbles of hydrogen on the zinc which makes subsequent washings more difficult. (c) The absolute ethanol and absolute ether washings were decanted directly on a Buchner funnel to prevent loss of the couple.

(5) The minimum time for effecting initiation has not been determined.

(6)(a) The reaction is essentially complete after 4–6 hours of refluxing. At this time the mixture assumes a dark red-brown color and precipitation of white zinc iodide is apparent. (b) The presence of active reagent from methylene iodide–zinc–copper can be determined conveniently by adding an aliquot to water and noting the volume of gases produced. (c) There were no differences apparent when these reactions were conducted under nitrogen or in the presence of air.

(7) The infrared spectra of the mixture indicated the absence of any methylene iodide.