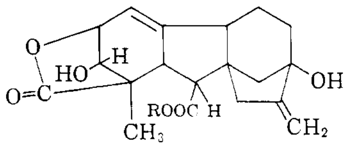
TABLE I

CHEMICAL AND PHYSICAL PROPERTIES OF SEVERAL *n*-ALKYL ESTERS OF GIBBERELLIN $A_3$ AND THEIR COMPARATIVE EFFECT ON GERMINATION OF LETTUCE SEED IN THE DARK



| R | Empirical Formula | Carbon % Calcd. | Carbon % Found | Hydrogen % Calcd. | Hydrogen % Found | M.P., °C. | Germination of Lettuce Seed, % |
|---|---|---|---|---|---|---|---|
| Control | | | | | | | 41.2[b] |
| H (Gibberellin $A_3$) | | | | | | | 80.6 |
| Methyl | $C_{20}H_{24}O_6$ | 66.6[a] | 66.2 | 6.7 | 6.6 | 202 | 63.5 |
| Ethyl | $C_{21}H_{26}O_6$ | 67.4[a] | 67.7 | 7.0 | 7.1 | 155 | 78.4 |
| *n*-Propyl | $C_{22}H_{28}O_6$ | 68.0 | 67.9 | 7.3 | 7.5 | 138 | 68.9 |
| *n*-Butyl | $C_{23}H_{30}O_6$ | 68.6[a] | 68.5 | 7.5 | 7.6 | 145 | 83.7 |
| *n*-Amyl | $C_{24}H_{32}O_6$ | 69.2 | 69.0 | 7.7 | 7.7 | 165–66 | 79.1 |
| *n*-Hexyl | $C_{25}H_{34}O_6$ | 69.7 | 69.5 | 7.9 | 7.9 | 188–89 | 56.8 |
| *n*-Heptyl | $C_{26}H_{36}O_6$ | 70.2 | 70.1 | 8.2 | 8.2 | 181–82 | 57.2 |
| *n*-Octyl | $C_{27}H_{38}O_6$ | 70.7[a] | 70.6 | 8.4 | 8.4 | 157–58 | 48.0 |
| *n*-Nonyl | $C_{28}H_{40}O_6$ | 71.2 | 71.5 | 8.5 | 8.9 | 131–32 | 46.7 |
| *n*-Decyl | $C_{29}H_{42}O_6$ | 71.6 | 71.6 | 8.7 | 8.8 | 102.5–108.5 | 40.0 |

[a] *Cf.* ref. (8). [b] L.S.D. at p. 05: 11.7. L.S.D. at p. 01: 16.4.

the dark may have resulted from hydrolysis of the esters to the acid (gibberellin $A_3$) in the aqueous germinating medium or hydrolysis within the seed or seedling after imbibition.

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## Chloromethylation of 1,2,4-Trimethylbenzene

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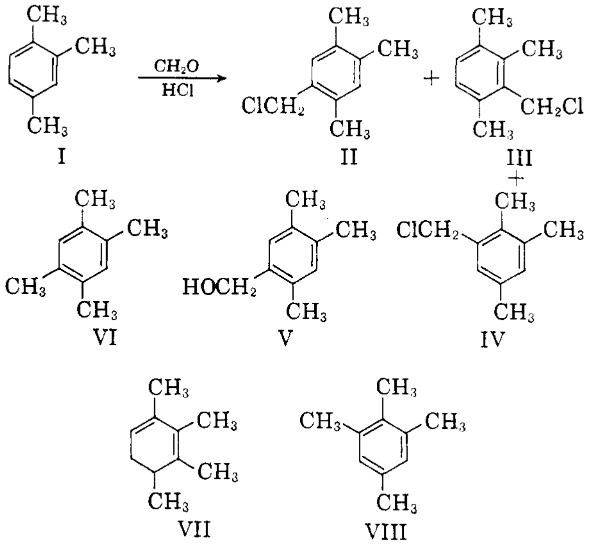
Previous investigators[1,2] of the chloromethylation of 1,2,4-trimethylbenzene (I) reported the product to be 2,4,5-trimethylbenzyl chloride (II). We have found the product, obtained in 78% yield, to be a mixture of 75% of 2,4,5-trimethylbenzyl chloride (II), 22% of 2,3,6-trimethylbenzyl chloride (III) and 2% of 2,3,5-trimethylbenzyl chloride (IV). The mixture boiled over a range of 3° and all fractions showed essentially identical refractive indices and infrared spectra. The mixture was nonseparable by vapor phase chromatography.



From the hydrolyzed chloride mixture was isolated 2,4,5-trimethylbenzyl alcohol (V, m.p. 81–82°) whose identity was confirmed by reduction to 1,2,4,5-tetramethylbenzene (VI). Authentic 2,4,5-trimethylbenzyl chloride (II) obtained from 2,4,5-trimethylbenzyl alcohol (V) showed a refractive index which was similar, but an infrared spectrum which was different, from that of the original mixture. Using authentic II as standard, the infrared spectrum of the original mixture indicated the presence of 74% of II.

The chloride mixture was further characterized by catalytic reduction to a mixture of tetramethylbenzenes whose infrared spectrum showed the presence of 76% of 1,2,4,5-tetramethylbenzene (VI), 22% of 1,2,3,4-tetramethylbenzene (VII) and 2% of 1,2,3,5-tetramethylbenzene (VIII). The analytical value for VI was obtained by direct com-

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(1) L. I. Smith and C. W. MacMullen, *J. Am. Chem. Soc.*, **58,** 629 (1936).

(2)(a) G. Vavon and J. Bolle, *Compt. rend.*, **204,** 1826 (1937); *Bull. soc. chim.* (5), **6,** 1025 (1939). (b) W. John and P. Günther, *Ber.*, **74B,** 879 (1941) report that chloromethylation of pseudocumene under conditions similar to our own, gives in addition to the main product (b.p. 98–108°/1 mm.), a by-product, $C_{11}H_{14}Cl_2$, b.p. 120–130°/1 mm., m.p. 99–101°. The latter is presumably an isomeric α,α′-dichloropentamethylbenzene.

parison with the spectrum of an authentic sample. The values for VII and VIII were obtained using bands corresponding to those of published spectra,[3] assuming the mixture to contain only VI, VII, and VIII, as evidenced by elemental analysis and molecular weight.

Permanganate oxidation of the initial mixture of benzyl chlorides gave 1,2,4,5-benzenetetracarboxylic acid in 36% yield.

## EXPERIMENTAL

The melting and boiling points are uncorrected.

*Chloromethylation of 1,2,4-trimethylbenzene.*[4] A mixture of 240 g. (2.0 mol.) of 1,2,4-trimethylbenzene (I), 178 g. (2.2 mol.) of formalin and 1250 ml. of concentrated hydrochloric acid was stirred for 6 hr. at 60–65° in the presence of a slow stream of hydrogen chloride. The product was extracted with petroleum ether (b.p. 40–45°) and the extract washed successively with water, aqueous bicarbonate and water, dried, and concentrated. The concentrate was distilled through a 13-cm. Vigreux column, and the major fraction (289 g., b.p. 40–105°/1.1 mm.) redistilled through a 50-cm. Vigreux column to yield 264 g. (78%) of trimethylbenzyl chloride; b.p. 106–109°/6 mm., $n_D^{25}$ 1.5410 (lit.[1] b.p. 111–116°/6 mm.).

*Anal.* Calcd. for $C_{10}H_{13}Cl$: C, 71.21; H, 7.77; Cl, 21.02. Found: C, 71.43; H, 7.81; Cl, 20.99.

A solid fraction (31.5 g., 7% yield, b.p. 99–112°/0.05 mm.) obtained in the first distillation was crystallized from *n*-hexane to give 8.0 g. of white solid (m.p. 83–83.5°), presumably an $\alpha,\alpha'$-dichloropentamethylbenzene.[2b]

*Anal.* Calcd. for $C_{11}H_{14}Cl_2$: C, 60.84; H, 6.50; Cl, 32.66; mol. wt., 217.1. Found: C, 60.90; H, 6.71; Cl, 32.76; mol. wt., 213.

*2,4,5-Trimethylbenzyl alcohol* (V). A mixture of 16.9 g. (0.10 mol.) of trimethylbenzyl chloride, 11.0 g. (0.10 mol.) of sodium carbonate and 100 ml. of water was refluxed for 12 hr. The crude product which separated on cooling (14.5 g., 97% yield, m.p. 51–75°) was crystallized from *n*-hexane to yield 5.2 g. (35%) of silky white needles of 2,4,5-trimethylbenzyl alcohol (V, m.p. 83–83.5°, lit.[1] m.p. 83–83.5°).

*Anal.* Calcd. for $C_{10}H_{14}O$: C, 79.95; H, 9.40. Found: C, 79.92; H, 9.17.

*2,4,5-Trimethylbenzyl N-phenylcarbamate.* The carbamate, m.p. 98–99°, was obtained as white needles by crystallization from petroleum ether (b.p. 40–45°).

*Anal.* Calcd. for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found: C, 76.02; H, 7.16; N, 5.22.

*Bis-trimethylbenzyl ether.* Concentration of the mother liquor from the crystallization of 2,4,5-trimethylbenzyl alcohol yielded 7.7 g. of semisolid, 2.0 g. of which was chromatographed on a silica gel column to give 1.0 g. of a chloroform-eluted fraction, m.p. 80–90°. Crystallization of the eluate from *n*-hexane gave white plates, m.p. 99.5–100.5°, presumably a bis-trimethylbenzyl ether.

*Anal.* Calcd. for $C_{20}H_{26}O$: C, 85.05; H, 9.28. Found: C, 84.82; H, 9.37.

The remaining fractions were oily and the only identified product isolated therefrom was 0.10 g. of 2,4,5-trimethylbenzyl alcohol.

*Reduction of 2,4,5-trimethylbenzyl alcohol to 1,2,4,5-tetramethylbenzene.* To a suspension of 3.76 g. (0.025 mol.) of 2,4,5-trimethylbenzyl alcohol in 100 ml. of liquid ammonia and 3.5 g. of absolute ethanol was added, during 45 min., 1.8 g. (0.075 g.-atom) of sodium. After evaporation of the ammonia the product was decomposed with ice and extracted with ether. The extract was concentrated and the residue washed with ethanol. The product (2.70 g., 81% yield) was crystallized from ethanol; melting point and mixture melting point with an authentic specimen 80–81° (lit.[5] m.p. 80°).

*2,4,5-Trimethylbenzyl chloride* (II). (A). A mixture of 6.81 g. (0.045 mol.) of 2,4,5-trimethylbenzyl alcohol (V) and 150 ml. of concentrated hydrochloric acid was stirred for 0.5 hr. at 25° followed by extraction with petroleum ether (b.p. 40–45°). The extract was washed, dried, concentrated, and the residue distilled to yield 6.47 g. (85%) of 2,4,5-trimethylbenzyl chloride (II); b.p. 108–109°/6.3 mm., $n_D^{25}$ 1.5400.

(B) A warm solution of 6.81 g. (0.045 mol.) of 2,4,5-trimethylbenzyl alcohol (V) in 50 ml. of benzene was added during 20 min. to a solution of 6.50 g. (0.054 mol.) of thionyl chloride and 5.4 g. (0.068 mol.) of pyridine in 25 ml. of benzene. After refluxing for 1 hr. the benzene layer was decanted from a small semisolid residue, washed successively with water, aqueous bicarbonate and water, dried and concentrated. Distillation of the residue yielded 5.12 g. (68%) of 2,4,5-trimethylbenzyl chloride (II); b.p. 111–112°/6.8 mm., $n_D^{25}$ 1.5399. The infrared spectra of the products obtained by methods A and B were identical.

*Anal.* Calcd. for $C_{10}H_{13}Cl$: C, 71.21; H, 7.77; Cl, 21.02. Found: C, 71.06; H, 7.57; Cl, 20.86.

*Reduction of trimethylbenzyl chloride mixture.* A solution of 16.8 g. (0.10 mol.) of the above mixture in 100 ml. of dioxane was hydrogenated at 25° under an initial pressure of 60 p.s.i. in the presence of 14.5 g. (0.12 mol.) of dimethylaniline and 0.5 g. of 10% palladiumized charcoal. The theoretical hydrogen uptake was reached in 2 hr. Dimethylaniline hydrochloride (16.6 g., 105% of theory, m.p. 82.5–86.5°) was recovered from the filtrate. The filtrate was concentrated and the residue dissolved in petroleum ether (b.p. 40–45°). The solution was washed successively with dilute hydrochloric acid, water, aqueous bicarbonate, dried, concentrated, and the residue distilled to yield 9.55 g. (71%) of a mixture of tetramethylbenzenes, b.p. 105–111°/49 mm.

*Anal.* Calcd. for $C_{10}H_{14}$: C, 89.49; H, 10.51; mol. wt., 134.2. Found: C, 89.49; H, 10.57; mol. wt., 137.

Quantitative infrared analysis of the tetramethylbenzene mixture showed 76% of VI, 22% of VII, and 2% of VIII. The bands appearing at 868, 804, and 847 cm.$^{-1}$ were used. These correspond to the literature values[3] of 867, 805, and 848 cm.$^{-1}$ for VI, VII, and VIII, respectively.

Crystallization of the mixture of tetramethylbenzenes from ethanol yielded colorless plates of 1,2,4,5-tetramethylbenzene (VI); melting point and mixture melting point with an authentic specimen 79–80° (lit.[5] m.p. 80°).

*1,2,4,5-Benzenetetracarboxylic acid.* A mixture of 8.43 g. (0.05 mol.) of the initial trimethylbenzyl chloride product, 5.3 g. (0.05 mol.) of sodium carbonate and 250 ml. of water was stirred and refluxed for 10 hr. while 79.0 g. (0.50 mol.) of potassium permanganate was added. Manganese dioxide was removed by filtration and excess permanganate in the filtrate destroyed with bisulfite. The filtrate, acidified with hydrochloric acid, was concentrated to 75 ml. and cooled to yield 8.66 g. of white crystals, m.p. >360°. Recrystallization of the product from dilute hydrochloric acid yielded 5.18 g. (36%) of 1,2,4,5-benzenetetracarboxylic acid dihydrate; m.p. 262–265°, lit.[6] m.p. 264°. Water of hydration was determined by heating to constant weight at 65°/0.05 mm.

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(3) American Petroleum Institute, Research Project 44, Carnegie Institute of Technology, Pittsburgh, Pa., *Catalog of Infrared Spectral Data*, Ser. No.'s 1592, 1295, 1591.

(4) Obtained from A. D. Little Co., 95.5% pure by ultraviolet analysis.

(5) L. I. Smith, *Org. Syntheses*, **Coll. Vol. II**, 248 (1943).

(6) G. Schroeter, *Ber.*, **57**, 2003 (1924).

*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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[2] H. A. Krebs, *Advances in Enzymology*, **3**, 191 (1943).

[3] H. L. Riley, J. F. Morley, and N. A. C. Friend, *J. Chem. Soc.*, 1875 (1932).

[4] N. Rabjohn, *Org. Reactions*, **V**, 331 (1947).

[5] E. J. Corey and J. P. Schaefer, *in press.* See also abstracts of the Sixteenth National Organic Chemistry Symposium of the American Chemical Society, p. 65 (1959).

[6] B. B. Corson, R. A. Dodge, S. A. Harris, and R. K. Hazen, *Org. Syntheses*, VIII, 68 (1928).

[7] I. Heilbron, *Dictionary of Organic Compounds*, Vol. I, 262 (1953).

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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).