Reaction of Organometallic Compounds with Propiolactone

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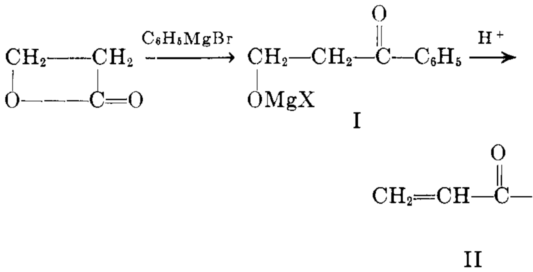
Received February 26, 1963

When propiolactone reacts with excess RLi compounds 1,1-disubstituted 1,3-propanediols are formed. Organocadmium compounds react with propiolactone to form 3-substituted propanoic acids as do benzylmagnesium chloride, benzyllithium, and allylmagnesium bromide. In general, organomagnesium compounds yield alkyl or aryl vinyl ketones.

Previous studies by Gresham and co-workers[2] have shown that phenylmagnesium bromide attacks propiolactone at the acyl carbon atom to give phenyl vinyl ketone (II) apparently through spontaneous dehydration of the intermediate β-hydroxypropiophenone (I).



On the other hand, benzylmagnesium chloride attacks propiolactone at the β-carbon atom to yield 4-phenylbutanoic acid. In both cases the production of polymeric substances and 3-halopropanoic acid accompanied carbon–carbon bond formation.

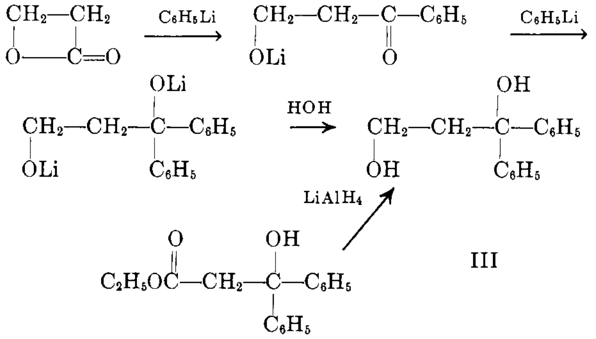
The present paper reports the reaction of other RM compounds with propiolactone.

The relatively low activity of organocadmium compounds toward carbonyl groups[3] suggested that the organocadmium compounds might provide a general method for the synthesis of substituted propanoic acids from propiolactone. Table I of the Experimental section shows that a variety of organocadmium compounds give fair to good yields (30–70%) of substituted propanoic acids. It is of interest to note that di-1-naphthylcadmium failed to react with propiolactone, whereas the 2-naphthyl derivative gave 3-(2-naphthyl)-propanoic acid. Implication of steric factors is suggested by the further observations that di-*o*-tolylcadmium gives a very low yield of acid and dimesitylcadmium gives no acid at all. Similarly, di-*t*-butylcadmium, prepared at −70°, failed to yield 4,4-dimethylpentanoic acid. The latter result may be due to the thermal instability of di-*t*-butylcadmium. Di-*t*-butylcadmium gives a 17% yield of methyl *t*-butyl ketone when treated with acetyl chloride at −70°.[3]

Allylmagnesium bromide, diphenylzinc, and benzyllithium behaved like benzylmagnesium chloride in that they gave carbon–oxygen cleavage to produce the corresponding acids.

When phenyllithium reacted with one equivalent of propiolactone, there was formed in addition to phenyl vinyl ketone, 1,1-diphenyl-1,3-propanediol (III). The structure of the latter product was established by an independent synthesis *via* reduction of ethyl 3-hydroxy-3,3-diphenylpropanoate[4] with lithium aluminum hydride. When two equivalents of butyllithium were used the diol was the sole product of the reaction. The reaction of a second mole of an RLi compound with a preformed lithium salt finds precedent in the halogen–metal interconversions with alcohols,[5] phenols,[6] and amines[7] and RLi exchange reactions with triarylsilanols.[8]

The reaction of organocadmium compounds with propiolactone appears to be a general method for preparing substituted propanoic acids.



Experimental

Reaction of Phenyllithium with Propiolactone.—Phenyllithium was prepared from lithium and bromobenzene in anhydrous ether.[9] To 0.1 mole of phenyllithium in 100 ml. of anhydrous ether, cooled to 0° in an ice–water bath, was added dropwise with rapid stirring 7.2 g. (0.1 mole) of propiolactone in 50 ml. of ether. A heavy, white precipitate appeared during the addition. After addition was complete, the mixture was decomposed with 35 ml. of water. The water layer, acidified to congo red with hydrochloric acid, yielded no acidic product.

A white solid which crystallized from the ether layer was filtered, washed with a small amount of ether, and dried. The yield of 1,1-diphenyl-1,3-propanediol was 4.6 g. (40% based on phenyllithium); m.p. 135–136°.

Anal. Calcd. for $C_{15}H_{16}O_2$: C, 78.9; H, 7.02; mol. wt., 228. Found: C, 78.7; H, 7.15; mol. wt., 225.

The filtrate from which the propanediol was removed yielded, on distillation, 5 g. (45%) of phenyl vinyl ketone identified as the pyrazoline.[2]

An authentic sample of 1,1-diphenyl-1,3-propanediol was prepared as follows: To a mixture of 0.5 g. of lithium aluminum hydride and 50 ml. of dry ether was added 2.7 g. (0.01 mole) of ethyl 3-hydroxy-3,3-diphenylpropanoate. The mixture was stirred and refluxed for 3 hr. The mixture was decomposed with wet ether and then treated with 20 ml. of 5% hydrochloric acid. The ether layer was separated and evaporated to dryness. Crystallization of the residue from ethanol yielded 1.6 g. (70%) of 1,1-diphenyl-1,3-propanediol melting at 134–135°. A mixture melting point with the product from the reaction of phenyllithium with propiolactone was 135–136°.

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[1] Chemistry Department, New Mexico Highlands University.

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TABLE I

RX	Product	M.p., °C.	Yield, %[a]
Bromobenzene	3-Phenylpropanoic acid	48.5–49[b]	77
3-Bromotoluene	3-(3′-Tolyl)propanoic acid	43–44.5[c]	51
2-Bromotoluene	3-(2′-Tolyl)propanoic acid	102–104[d]	5
2-Bromonaphthalene	3-(2′-Naphthyl)-propanoic acid	134–135[e]	48
1-Bromonaphthalene	No reaction		
Bromomesitylene	No reaction		
2-Iodothiophene	3-(2′-Thenyl)-propanoic acid	45–46.5[f]	41
1-Bromobutane	Heptanoic acid	(B.p.) 222	32[g]
2-Chloro-2-methylpropane	No reaction[h]		

[a] Based on propiolactone. [b] F. F. Blicke and D. G. Sheets, *J. Am. Chem. Soc.*, **70**, 3768 (1948). [c] V. Miller and H. Rohde, *Ber.*, **23**, 1899 (1890). [d] C. Grundman, *ibid.*, **81**, 513 (1948). [e] R. T. Arnold and R. Barnes, *J. Am. Chem. Soc.*, **65**, 2393 (1943). [f] G. Barger and A. P. T. Easson, *J. Chem. Soc.*, 2100 (1938). [g] Melting point of the anilide, 71°. R. L. Shriner and R. C. Fuson, "Identification of Organic Compounds," 4th Ed., John Wiley and Sons, Inc. New York, N. Y., 1956, p. 276. [h] Reaction carried out at −70°.

1,1-Di-*o*-anisyl-1,3-propanediol.—When *o*-anisyllithium was treated with propiolactone a 60% yield of 1,1-di-*o*-anisyl-1,3-propanediol, m.p. 105° (from ethanol), was obtained.

Anal. Calcd. for $C_{17}H_{20}O_4$: C, 70.8; H, 6.94. Found: C, 70.9; H, 6.91.

Benzyllithium with Propiolactone.—When one equivalent of benzyllithium[10] was cooled to 0° and treated with one equivalent of propiolactone, there was obtained, subsequent to hydrolysis and acidification, a 65% yield of 4-phenylbutanoic acid, identified by mixture melting point.[11]

Diphenylzinc with Propiolactone.—A solution of diphenylzinc[12] was cooled to 0° and treated dropwise with an equivalent of propiolactone. After hydrolysis and acidification there was obtained a 40% yield of 3-phenylpropanoic acid, m.p. 48°.

Allylmagnesium Bromide with Propiolactone.—To a solution of 0.1 mole of allylmagnesium bromide in 100 ml. of anhydrous ether, cooled to 0°, was added dropwise, with stirring, 7.2 g. (0.1 mole) of propiolactone in 50 ml. of anhydrous ether. After addition was complete the mixture was hydrolyzed with aqueous ammonium chloride. The aqueous layer was acidified with hydrochloric acid and extracted with three 50-ml. portions of ether. The combined ether extracts were dried over sodium sulfate and then subjected to distillation. The yield of 5-hexenoic acid, boiling at 202°, was 6.2 g. or 54%; $d^{25}{}_{25}$ 1.011; neut. equiv., 111.

Organocadmium Compounds.—General procedure: To 0.1 mole of the Grignard reagent in 100 ml. of anhydrous ether was added 19.1 g. (0.05 mole) of cadmium chloride. When color test I[13] was negative the ether solution was decanted into a second reaction flask. A 10-ml. aliquot was hydrolyzed with distilled water and titrated with 0.1 N hydrochloric acid to the methyl orange end point. The organocadmium solution was then cooled to 0° and one equivalent of propiolactone was added. After addition was completed the mixture was hydrolyzed with water, the aqueous layer acidified with concentrated hydrochloric acid, and the reaction product isolated by extraction with ether followed by distillation or crystallization from an appropriate solvent. Table I summarizes the results.

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Spectral Studies of the "d^6" Metalloporphyrins. Ligand and Solvent Field Effects on Ferrous and Cobaltic Mesoporphyrin IX[1]

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Received March 14, 1963

A new method for the preparation of ferrous mesoporphyrin IX has made possible the study of this complex under a variety of new conditions. The ferrous complexes, prepared in this manner, should serve as much better models for biological systems than those previously reported. The effect of solvents on the visible- and near-ultraviolet spectra of the cobalt mesoporphyrins has been investigated extensively. A profound solvent effect on the oxidation–reduction potentials of the cobalt porphyrins has been observed. These results have been interpreted with the aid of ligand field theory.

In the studies of the absorption spectra of metalloporphyrins especial significance has been attached to the relative intensities of the absorption bands. Since the intensities of the bands as well as their positions vary greatly with solvent, a detailed study of solvent–spectral relationships has been needed. Spectral studies of the ferrous complexes with simple molecules (dimethylglyoxime, phenanthroline, etc.), ferrous porphyrin complexes with proteins, and ferrous complexes of the porphyrins in the presence of nitrogenous bases (pyridine, ammonia) have been reported.[4] However, there exists very little data on the spectra of simple ferrous porphyrins owing to their marked instability in air and the difficulties in their preparation. The simple porphyrin complexes that have been prepared have usually been associated with powerful ligands capable of producing profound effects of their own in addition to the effect of the porphyrin ring. Common reducing agents employed in the preparation of ferrous porphyrin complexes (*i.e.*, hydrazine and dithionite) can serve as ligands, making it difficult to separate the spectral effects produced by these ligands.

Ferrous ion, with six d electrons, can exist either in a low spin configuration with no unpaired electrons or in a high spin configuration with four unpaired electrons; ferric ion can have one or five unpaired electrons. According to ligand field theory, ferric ion should exist in the high spin configuration except in the presence of

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[1] Porphyrin Studies XXVII. Paper XXVI, A. H. Corwin, *Trans. N. Y. Acad. Sci.*, **25**, 569 (1963); this work was supported in part by NIH grant A-2877(C3).

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