

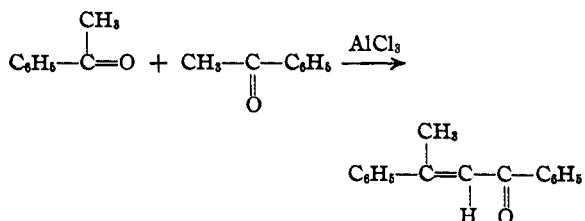
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, FISK UNIVERSITY]

Reactions in the Presence of Metallic Halides. I. β -Unsaturated Ketone Formation as a Side Reaction in Friedel-Crafts AcylationsBY N. O. CALLOWAY¹ AND LOUIS D. GREEN

Often directions for the preparation of ketones by the Friedel-Crafts method from a hydrocarbon and an acid halide specify a reaction period of such length that hydrogen halide evolution ceases. These statements lead to ambiguous reaction conditions. A major difficulty is the problem of determining the point at which the hydrogen halide evolution stops. On the one hand, experience has shown that the reaction is seldom complete when there is no longer visible bubble formation at room temperature. On the other hand, it is not possible to discern bubble formation during reflux especially if low-boiling solvents are used.² Yet the ordinary test with ammonia shows *some* evolution of hydrogen halide *as long as the reaction mixture is refluxed*.

It has further been noted that prolonged reflux or extended reaction time actually decreases the yield of ketone beyond a certain period. This decrease in ketone is accompanied by an increase in the formation of high-boiling oxygen containing substances.

In an effort to find, if possible, a method that would minimize the loss of ketone by reaction subsequent to formation, it was observed in the synthesis of acetophenone that the residues consisted primarily of dypnone which had resulted from the condensation of two molecules of acetophenone.



Closer examination of this reaction revealed the fact that it is one that will take place to an extent approximating completeness only when the ketone is present in excess of molar quantities as compared with the aluminum chloride. Two moles of acetophenone per mole of aluminum chloride gave the highest yields (73%). Quan-

ties of aluminum chloride in excess of 1 mole per mole of acetophenone were essentially without effect in bringing about the reaction. Any excess of simple ketone beyond 2 moles tended to produce high molecular weight, viscous gums, and to reduce markedly the yield of dypnone. At low temperatures the condensation proceeds quite slowly and the formation of the gummy residues which are always present in small quantities when the reaction takes place at room temperature is strongly inhibited. At 40-50° the time for the reaction is shortened and the residue is markedly increased. Stirring has little effect.

Although hydrogen chloride is evolved continually during any period of heating of acetophenone and aluminum chloride, the simple explanation that the condensation is promoted by hydrogen halide is not tenable. This general type of condensation may be promoted by hydrogen halides,³ it is true, but also by alkalis,⁴ heat,⁵ radiation,⁶ zinc alkyls,⁷ organoaluminum halides,⁸ acetic anhydride,⁹ sulfuric acid,⁹ sodium pyrosulfate,¹⁰ sodamide,¹¹ and aluminum and alkyl halides.¹²

The fact that the three valences of aluminum in aluminum chloride are occupied by chlorine atoms seemed incidental to the process of condensation. Therefore, a substance such as triphenylaluminum, in which the three valences are occupied by non-haloid groups, should bring about this condensation.¹³ It was found that triphenylaluminum did condense acetophenone to yield dypnone although a portion of the organometallic compound reacted with the car-

(3) Cologne, *Bull. soc. chim.*, [4] **49**, 426 (1931); Grignard and Cologne, *Bul. soc. chim. Romania*, **15**, 5 (1933); [*C. A.*, **28**, 101 (1934)].

(4) Kohler, "Organic Syntheses," Coll. Vol. I, 1932, p. 71.

(5) Mitchell and Reid, *THIS JOURNAL*, **53**, 336 (1931).

(6) Clark and Pickett, *ibid.*, **52**, 468 (1930).

(7) Delacre, *Bull. acad. roy. belg.*, [3] **22**, 470 (1892); [*Brit. Chem. Abstracts*, **62**, 993 (1892)].

(8) Leone and Braicovic, *Gazz. chim. ital.*, **55**, 301 (1925); [*C. A.* **19**, 2929 (1925)].

(9) Claisen and Claparède, *Ber.*, **14**, 2464 (1881).

(10) Odell and Hines, *THIS JOURNAL*, **35**, 83 (1913).

(11) Haller and Bauer, *Ann. chim.*, [8] **28**, 409, 413 (1913).

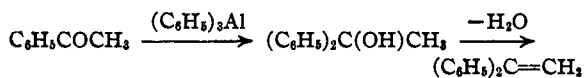
(12) Konowalow and Finogjew, *J. Russ. Phys.-Chem. Soc.*, **34**, 945 (1902); [*Brit. Chem. Abstracts*, [1] **84**, 264 (1903)].

(13) Gilman and Nelson, *Rec. trav. chim.*, **55**, 522, 527 (1936).

(1) This work was initiated while one of us was a faculty member at Tuskegee Institute.

(2) Calloway, *Chem. Rev.*, **17**, 327 (1935).

bonyl group. No methylphenylcarbinol was observed. There was isolated, however, a substance which gave every indication of being *as*-diphenylethylene. There was a residue of



resinous material that undoubtedly resulted from further condensation of the β -unsaturated ketone.

From the general effectiveness of aluminum alcoholates as condensing agents, it may be that in both the case of aluminum chloride and of triphenylaluminum there was an intermediate formation of substances of the general type of R-O-Al-R_2 which actually promoted the condensation. Thus in the case of aluminum chloride, the aluminum salt may have been formed from the enol of acetophenone. From triphenylaluminum the salt may arise either by reaction with enolic acetophenone or more likely directly by reaction of triphenylaluminum with the acetophenone.

When benzaldehyde was substituted for one mole of the acetophenone and condensation was brought about by aluminum chloride, chalcone was isolated in excellent yields (91%). It is noteworthy here that the reaction proceeded more rapidly than when dyprnone was formed.

Experimental Part

Dyprnone from Ketone Synthesis.—To 13.3 g. (0.1 mole) of anhydrous aluminum chloride in 100 cc. of dry carbon disulfide in a 500-cc. three-necked balloon flask equipped with a mercury-sealed mechanical stirrer, a dropping funnel, and a reflux condenser closed by a tube of calcium chloride leading to a suitable trap, there was added dropwise 7.8 g. (0.1 mole) of redistilled acetyl chloride taking care that the temperature did not rise above 25°. After the resulting oily complex had stirred for fifteen minutes, there was added dropwise 7.8 g. (0.1 mole) of dry, thiophene-free benzene over a period of twenty minutes. The reaction was stirred for one hour, after which it was refluxed and stirred for twelve hours. Hydrogen chloride was evolved during this entire period, rapidly at first and more slowly toward the end of the reaction.

The dark brown, viscous reaction mixture was poured over 200 g. of crushed ice. The aqueous layer was separated and extracted with two 25-cc. portions of carbon disulfide. The washings were combined with the original carbon disulfide layer and washed with two portions of water and one of 10% sodium bicarbonate. After drying over sodium sulfate the solvent was removed on a water-bath.

Vacuum fractionation yielded 8.4 g. (70%) acetophenone, b. p. 106–109° (38–40 mm.), and 3 g. of dyprnone, b. p. 160–165° (1 mm.). There was a gummy viscous residue of 1 g.

The dyprnone was identified by the semicarbazone which melted at 150–151° and showed no depression when mixed with a sample of known material.¹⁴

In a duplicate run which was heated for only three hours, 10.1 g. of acetophenone was obtained (83%). There was no dyprnone or residue.

Condensation of Acetophenone to Dyprnone.—For all reactions involving stirring or refluxing the set-up described for the acylation above was used. Heat was applied to the appropriate reactants by means of a water-bath on a hot-plate. For all reactions not involving stirring or refluxing, the following set-up was used. A suitably sized Erlenmeyer flask was equipped with a rubber stopper fitted with a large straight calcium chloride tube completely filled with coarse calcium chloride.

In all cases the acetophenone was added slowly to the aluminum chloride in carbon disulfide. During this addition considerable heat was evolved. Reflux of the solvent was avoided by cooling with running water; 100 cc. of carbon disulfide was used for each tenth mole of aluminum chloride. *In every case hydrogen chloride was evolved throughout the reaction period.*

The products were isolated by the procedure given for the isolation of dyprnone from the ketone synthesis above. Systematic variation of conditions showed that the best yields of dyprnone were obtained when two moles of acetophenone were added to one mole of aluminum chloride at room temperature and allowed to stand for seven days, yield 73%.

The Synthesis of Chalcone.—Using essentially the same procedure as that outlined for dyprnone chalcone was prepared by adding 12.1 g. (0.1 mole) of acetophenone to 13.3 g. (0.1 mole) of aluminum chloride in 100 cc. of carbon disulfide keeping the reaction cooled with tap water. After the resulting complex was formed, the reaction mixture was allowed to stand for thirty minutes with occasional shaking. There was then added slowly 10.6 g. (0.1 mole) of purified benzaldehyde. The flask was closed with a tube of calcium chloride and shaken occasionally during the first hour. It was then allowed to stand for four days. At the end of this time the liquid complex had solidified to definite yellow to brown crystals. The carbon disulfide was decanted and discarded. The crystals were washed with two portions of benzene and allowed to drain free of solvent by inverting the flask. Water was now added and the crystalline mass broken up with a stirring rod. When hydrolysis was complete the product was cooled in ice. The resulting yellow crystalline product was filtered off. After one crystallization from alcohol it melted at 54–56°, yield 19 g., 91% of theoretical. The m. p. of a sample mixed with an authentic specimen⁴ was 55–56°.

Hydrolysis of the entire reaction mixture without decanting the carbon disulfide, as for dyprnone, gave essentially the same results as obtained in the preceding chalcone run, when the product was distilled.

Reaction of Triphenylaluminum with Acetophenone.—Triphenylaluminum¹⁵ was prepared in toluene solution from diphenylmercury¹⁶ under nitrogen free from carbon dioxide, oxygen and moisture. To 190 cc. of a filtered solu-

(14) Wilson and Macaulay, *J. Chem. Soc.*, **125**, 841 (1924).

(15) Gilman and Marple, *Rec. trav. chim.*, **55**, 133 (1936).

(16) Nesmeyanow, *Ber.*, **62**, 1012 (1929); Nesmeyanow and Kahn, *ibid.*, **62**, 1018 (1929).

tion of 7.7 g. (0.03 mole) of triphenylaluminum in a three-necked flask fitted with an inlet for nitrogen, a mechanical stirrer and a reflux condenser closed by a tube filled sufficiently with sulfuric acid to assure a positive nitrogen pressure, there was added 12 g. (0.1 mole) of acetophenone. No immediate reaction was perceptible. After thirty minutes a flocculent precipitate appeared. The mixture was now heated in an oil-bath at 100–115° for six hours after which it was allowed to stand for six hours at room temperature. The thick, pasty reaction mixture was poured into 100 cc. of water containing 2% nitric acid. The toluene layer was separated, washed with water and 10% sodium bicarbonate and dried over sodium sulfate. The solvent was removed by distillation and the residue was twice vacuum fractionated at 9 mm. Two fractions were obtained: (A) b. p. 108–120°, 3 g.; (B) b. p. 190–195°, 4 g.; residue, 3 g. that did not distill up to 270°. This residue set to a hard amber colored resin-like mass soluble in acetone but sparingly soluble in alcohol and ether.

Fraction B.—Dyponne by m. p. and mixed m. p. of oxime,¹⁷ 133–134°.

Fraction A.—This material was shaken for fifteen hours with a saturated solution of sodium bisulfite to remove any ketone. The oil was then extracted with ether and dried over sodium sulfate. Distillation gave 2 g. of a product boiling at 272–277°; n_D^{14} 1.6070; 0.1 g. of this material in dry chloroform immediately discharged the color of bromine¹⁸ to form an addition product that evolved hydrogen bromide when the solvent was removed.

Oxidation¹⁸ of 0.8 g. of this oil at 80° for five hours gave

(17) Henrich and Wirth, *Ber.*, **37**, 731 (1904).

(18) Mulliken, "The Identification of Pure Organic Compounds," John Wiley and Sons, Inc., N. Y., Vol. I, First Edition, 1904, p. 194.

a product which when extracted from alkaline solution by ether would not crystallize at room temperature, but gave 1 g. of an oxime, melting¹⁸ (p. 150) at 140–141° and showing no depression of m. p. when mixed with a known sample of benzophenone oxime. It was concluded that the substance was α, α -diphenylethylene.

In a run in which acetophenone was refluxed with sodium-dried toluene for thirty-six hours, no dyponne was found.

The authors are grateful to Mr. Thomas Campbell who kindly prepared some of the starting materials.

Summary

1. The evolution of hydrogen halide in the Friedel–Crafts ketone synthesis is not a satisfactory criterion for judging the optimum period of reaction.

2. Drastic and prolonged reaction conditions and especially the use of an insufficient proportion of aluminum chloride tend to encourage condensation of ketones primarily formed by acylation.

3. Aluminum chloride is capable of condensing acetophenone to form dyponne and a mixture of acetophenone and benzaldehyde to form chalcone.

4. Triphenylaluminum similarly will produce dyponne from acetophenone.

NASHVILLE, TENN.

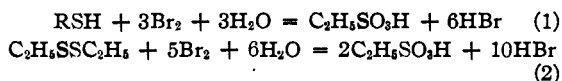
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[CONTRIBUTION FROM THE DIVISION OF CHEMISTRY, COLLEGE OF AGRICULTURE, UNIVERSITY OF CALIFORNIA]

Oxidation of Ethyl Mercaptan and Ethyl Disulfide by Bromine in the Presence of Water

By H. A. YOUNG

Dilute carbon tetrachloride solutions of ethyl mercaptan and ethyl disulfide are oxidized in a normal manner¹ to ethyl sulfonic acid by bromine water, as represented by the equations



Ethyl mercaptan is converted instantaneously and quantitatively to the disulfide in the absence of water, in accord with the results of Otto and Rossing.²

(1) It is well known that strong oxidizing agents convert mercaptans and disulfides to the corresponding sulfonic acids. Friedman [*Beitr. Chem. Physiol. Path.*, **3**, 25, 38 (1903)] has shown that bromine oxidizes cystine and cysteine to cysteic acid.

(2) Otto and Rossing, *Ber.*, **19**, 3136 (1886).

Experimental Part

Equivalents of Bromine Used per Mole of Sulfur Compound

Ethyl Mercaptan.—Carbon tetrachloride solutions of the mercaptan were prepared and analyzed just before use by the iodimetric method of Reid.³ A measured volume of mercaptan solution (approximately 0.005 *M*) was introduced into a 250-cc. glass-stoppered flask containing 100 cc. of water and a measured volume of a known solution of bromine (excess) in carbon tetrachloride was added immediately. The flasks were then put in a shaker in a 25° thermostat, and after various times were withdrawn, 2 g. of solid potassium iodide added, and the liberated iodine was titrated with 0.1 *N* sodium thiosulfate solution. The results of a series of such experiments showed that 6.00 \pm 0.03 equivalents of bromine were used per equivalent of

(3) Sampey and Reid, *This Journal*, **54**, 3405 (1932).