to the extent of about 1 g. in 100 cc. of the boiling solvent, but is almost insoluble in the cold.

Anal. Found: C, 83.99, 83.95, 83.89, 84.10, average 83.98; H, 6.84, 6.69, 6.78, 6.84, average 6.79; N, 8.90, 8.92, 9.14, 9.25, average 9.05; molecular weight (Rast method), 287, 303. Calcd. for $C_{21}H_{20}N_2$: C, 83.96; H, 6.79; N, 9.33; mol. wt., 300.4. For $C_{22}H_{22}N_2$: C, 84.04; H, 7.05; N, 8.91; mol. wt., 314.4.

A. Attempted Hydrolysis.—After heating 0.1448 g. of the compound in 10 cc. of concentrated hydrochloric acid for one hour at 70–90°, there was recovered 0.1450 g. of material of unchanged melting point. After refluxing overnight at the boiling point of the acid, most of the material was recovered unchanged. Likewise, more than 90% of the material was recovered, with but slightly lowered melting point, after refluxing the compound for six days in 10% aqueous potassium hydroxide solution. Similar lack of hydrolysis occurred through heating in a solution of potassium hydroxide in absolute alcohol.

B. Attempted Reduction.—After exposure of 0.5023 g. of the material melting at 96° to hydrogen in the presence of the Adams platinum catalyst for five days, there was recovered 0.284 g. of recrystallized material melting at 90–93°; the melting point of a mixture with the original compound was 94–95°. The initial compound was unaffected by action of tin and hot concentrated hydrochloric acid.

C. Attempted Oxidation.—Even after exposure of the compound to the action of a saturated solution of potassium permanganate in acetone at 55° for one week, solid, melting at 83–85°, was recovered and, upon purification, proved to be unchanged material. However, the action of an alkaline solution of potassium permanganate[9] resulted in the production of benzoic acid.

D. Bromination.—Preliminary trial indicated that the product melting at 96° decolorized a benzene solution of bromine, with evolution of hydrogen bromide, much more readily than did a benzene solution of 1-chloro-4-phenyl-2-butanone or 5-phenethyl-5-hydantoinacetonitrile.

Therefore, to 1.0 g. (0.0033 mole based on $C_{21}H_{20}N_2$) of the compound in benzene solution at room temperature was added a bromine solution containing 0.655 g. (0.0041 mole) of bromine. During most of the addition, the color due to bromine disappeared and hydrogen bromide was evolved. The solvent was removed by evaporation and the solid residue was recrystallized from diluted alcohol to yield 1.15 g. of material melting at 80–90°. Two further recrystallizations produced 0.89 g. melting at 101–102° (cor.).

Anal. Calcd. for $C_{21}H_{19}BrN_2$: mol. wt., 379.4; C, 66.50; H, 5.05; Br, 21.07; N, 7.39. Found: mol. wt. (Rast), 365; C, 66.74; H, 5.12; Br, 21.08; N, 7.48.

E. Action of Alcoholic Hydrogen Chloride.—Two grams of the compound melting at 96° was dissolved in 25 cc. of ethanol and the solution was heated under reflux on a steam-cone for twenty hours with continuous introduction of dry hydrogen chloride. Upon cooling, a semi-solid precipitate formed but could not be made to solidify completely. Hence, 20 cc. of concentrated hydrochloric acid was added and heating was continued for five hours. Subsequent cooling caused the separation of a small amount of solid and relatively a larger amount of an oily liquid. The latter, halogen-free but containing nitrogen, was heated for twelve hours with 30 cc. of 10% solution of sodium hydroxide in 50% alcohol. Upon cooling, there was obtained 1.35 g. of a solid, melting at 141–144°, which, after five recrystallizations from diluted alcohol and from benzene, produced 0.82 g. of material melting at 153.2–154.2° (cor.). The analytical data indicated that this treatment had caused hydration of the initial product.

Anal. Calcd. for $C_{21}H_{22}N_2O$: C, 79.21; H, 6.96; N, 8.80. Found: C, 79.22; H, 6.97; N, 8.68.

Summary

1. By slight modification of the Bucherer procedure, a 5,5-disubstituted hydantoin has been synthesized from an α-chloroketone. From the 5-phenethyl-5-hydantoinacetonitrile have been prepared the corresponding hydantoinacetic acid, its ethyl ester and its amide.

2. As a by-product in the synthesis of the hydantoinacetonitrile there was obtained a neutral, chemically rather non-reactive material, probably $C_{21}H_{20}N_2$, the structure of which is unknown, but certainly is not that of a hydantoin.

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[9] Shriner and Fuson, "Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1935, p. 139.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF MOUNT HOLYOKE COLLEGE]

Addition of Grignard Reagents to α,β-Unsaturated Aldehydes and Ketones. I. *trans*-3-Hepten-2-one

BY MARTHA E. SMITH, BARBARA CHASE[1] AND RUTH RHODES[1]

For an investigation of the influence of steric factors in determining the mode of addition of the Grignard reagent to the conjugated system present in α,β-unsaturated ketones, the extent of 1,4-addition of three different Grignard reagents to *trans*-3-hepten-2-one has been studied. This ketone has been prepared by dehydration of the corresponding ketol, 4-hydroxy-2-heptanone. The ketol was prepared according to the method of Eccott and Linstead.[2] The preparation of the *cis* isomer by the direct condensation of *n*-butyraldehyde and acetone has been reported by Eccott and Linstead,[2] but Powell and Ballard[3] have indicated that the product obtained in this reaction under the conditions used by Eccott and Linstead consists of a mixture of the unsaturated aldehyde, 2-ethyl-2-hexenal, and the *trans* form of 3-hepten-2-one. This reaction and the behavior of the product with Grignard reagents is under further investigation in this Laboratory.

According to Grignard and Dubien,[4] the reaction of 3-hepten-2-one with methyl-, ethyl-, *n*-propyl- and *n*-butylmagnesium halides gave only the 1,2-addition product, with no evidence of any 1,4-addition, while Colonge[5] reported 40% satu-

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[1] Part of the experimental work was done by Barbara Chase and Ruth Rhodes in partial fulfillment of the requirements for the degree of Master of Arts at Mount Holyoke College.

[2] Eccott and Linstead, *J. Chem. Soc.*, 905 (1930).

[3] Powell and Ballard, THIS JOURNAL, **60**, 1914 (1938).

[4] Grignard and Dubien, *Ann. chim.*, **2**, 282 (1924).

[5] Colonge, *Bull. soc. chim.*, [5] **3**, 413 (1936).

rated ketone, the 1,4-addition product, and 60% unsaturated tertiary alcohol when either the *trans* form of 3-hepten-2-one or the *cis* isomer, prepared according to the method of Eccott and Linstead, reacted with ethylmagnesium bromide.

In the present investigation the reactions of *trans*-3-hepten-2-one with ethyl- and isopropylmagnesium bromides and *t*-butylmagnesium chloride have been studied and the extent of 1,4-addition determined by the use of Girard reagent (betaine hydrazide hydrochloride). Preliminary experiments had shown that this reagent gives a satisfactory method for the quantitative determination of the ketone, and the results are reported on the basis of the weight of ketone obtained from the total weight of material recovered after treatment with Girard reagent. There has been no attempt to determine quantitatively the amount of unsaturated tertiary alcohol in the non-ketonic material, which would contain also any complex products resulting from the Grignard reaction. The ketonic fraction, in each case, has been shown to be a single compound, saturated to bromine and permanganate solution, and therefore is a measure of the extent of 1,4-addition to the unsaturated ketone.

The results, summarized in Table I, show that ethylmagnesium bromide gives the least amount of 1,4-addition, which would be expected since small aliphatic radicals (methyl and ethyl) tend to add directly to the carbonyl group of an aliphatic unsaturated ketone. However, it is most surprising, in view of this, that the isopropylmagnesium bromide is more reactive with respect to 1,4-addition than the *t*-butyl Grignard reagent. These differences are large enough to be of real significance, and are contrary to any previously reported results in which the behavior of different Grignard reagents with the same α,β-unsaturated carbonyl compound has been studied. In the work of Stevens[6] with crotonaldehyde and different Grignard reagents, only traces of 1,4-addition were found with ethyl- and isopropylmagnesium bromides, but *t*-butyl and *t*-amyl Grignard reagents gave 20.3 and 22.6% of 1,4-addition, respectively. Whitmore[7] found a gradual increase in the amount of 1,4-addition of the Grignard reagent to Δ^2-cyclohexenone as the size of the alkyl radical increased from methyl to *t*-butyl. It should be noted that in the first of these cases the unsaturated carbonyl compound is an aldehyde and in the other the reactivity of the carbonyl group more closely resembles that of an aldehyde than of an aliphatic ketone. However, if the variation in amount of 1,4-addition with increasing size and branching of the alkyl radical were due to a steric effect, it would seem reasonable to assume that the same order of reactivity would be observed with the 3-hepten-2-one. Kohler[8] showed that the amount of 1,4-addition to an α,β-unsaturated ketone did not vary much with Grignard reagents containing the methyl, ethyl and benzyl radicals, but that phenylmagnesium bromide gave a much smaller per cent. of 1,4-addition product. On the other hand, he stated that the extent of 1,4-addition with cyclohexylmagnesium bromide was greater than that observed with other Grignard reagents. From this it has been concluded that factors other than steric hindrance must influence the direction of addition to a conjugated carbonyl system. The results of the present investigation point to a similar conclusion.

TABLE I

SEPARATION OF PRODUCTS OF GRIGNARD REACTIONS

Grignard reagent	Product, g.	Ketone, g.	Non-ketonic product, g.	% Recovery	% Ketone
Ethyl	20.0	3.27	10.55	69.1	23.7
	20.0	4.32	12.06	81.9	26.3
	10.0	2.37	6.90	92.7	25.6
	10.0	1.70	6.20	79.0	21.5
	10.0	1.93	6.17	81.0	23.8
				Average	24.2
Isopropyl	20.0	8.90	9.90	94.0	47.4
	20.0	8.78	9.82	93.0	47.2
	20.0	8.00	9.66	88.3	45.4
	20.0	7.93	9.65	87.9	45.2
				Average	46.3
t-Butyl	10.0	3.34	5.96	93.0	35.9
	10.0	3.22	5.44	86.6	37.1
	10.0	3.30	6.68	99.8	33.1
	10.0	2.84	5.66	85.0	33.4
				Average	34.9

It is of interest to note that, of the above series of Grignard reagents, the cyclohexylmagnesium bromide is the only one derived from a secondary halide. In the present work, the isopropyl Grignard reagent, which gives an unusually large amount of 1,4-addition, is also derived from a secondary halide. This factor may be of significance in determining the direction of addition of a Grignard reagent to an α,β-unsaturated ketone.

Experimental

4-Hydroxy-2-heptanone.—This ketol was prepared by condensation of *n*-butyraldehyde with acetone, according to the method of Eccott and Linstead.[2] The fraction boiling at 90–97° at 20 mm. was collected in a yield of 80%.

***trans*-3-Hepten-2-one.**—The ketol, 4-hydroxy-2-heptanone (315 g., 2.4 moles) was dehydrated by refluxing for an hour on a steam-bath with a solution of 125 ml. of concentrated sulfuric acid in 250 ml. of water, rather than with oxalic acid, as in Eccott and Linstead's work.[2] The product was steam-distilled and separated from the aqueous layer, which was extracted with ether. The combined ether extracts and oil were dried with potassium carbonate, and the solvent removed under reduced pressure. The ketone was carefully fractionated through a modified Widmer column.[9] The yield of ketone (b. p. 59.5–60.5° at 16 mm., n^{20}_{D} 1.4421) was 87.1 g. The semicarbazone, after recrystallization from dilute ethanol, melted at 124–

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(6) Stevens, THIS JOURNAL, **57**, 1112 (1935).

(7) Whitmore and Pedlow, *ibid.*, **63**, 758 (1941).

(8) Kohler and Burnley, *Am. Chem. J.*, **43**, 412 (1910).

(9) Smith and Adkins, THIS JOURNAL, **60**, 662 (1938).

125°. The physical properties of the ketone and melting point of the semicarbazone agree with those of Eccott and Linstead.[2] The 2,4-dinitrophenylhydrazone, prepared according to the method of Allen[10] and recrystallized from 95% alcohol, melted at 125–126°. This is in accord with the value reported by Powell.[3]

Reaction of *trans*-3-Hepten-2-one with Ethylmagnesium Bromide.—The procedure was essentially that used by Whitmore.[7] Four reactions were carried out as follows: the ketone (56 g., 0.5 mole) in 200 ml. of ether was added to the Grignard reagent prepared from 109 g. (1 mole) of ethyl bromide and 24.2 g. of magnesium in 300 ml. of ether at 0° during a period of three hours with vigorous stirring, and stirring was continued for an hour longer. After standing overnight, the product was decomposed by pouring onto 1 kg. of cracked ice and 250 g. of ammonium chloride. The ether layer was separated, the water layer extracted several times with ether, and the combined extracts dried over sodium sulfate. The ether was distilled off under reduced pressure and the weight of the residue determined. The average yield was 84%.

Reaction of *trans*-3-Hepten-2-one with Isopropylmagnesium Bromide.—Two reactions were carried out according to the procedure used with ethylmagnesium bromide. The yield was 80%.

Reaction of *trans*-3-Hepten-2-one with *t*-Butylmagnesium Chloride.—Two reactions were carried out as follows: to 19.4 g. (0.8 mole) of magnesium in 500 ml. of ether was added, over a period of eight hours, 74 g. (0.8 mole) of *t*-butyl chloride dissolved in 200 ml. of ether. A crystal of iodine and a small amount of a reacting mixture of magnesium and *t*-butyl chloride in ether were added as catalysts and the reaction was carried out between 38 and 40°. Stirring was continued for an hour after the addition was completed. After the mixture had stood for twelve hours, it was packed in ice and 42.6 g. (0.4 mole) of *trans*-3-hepten-2-one in 200 ml. of ether solution was added with stirring during two and one-half hours. The mixture was allowed to stand overnight, and the product treated as in the reaction with ethylmagnesium bromide. The average yield from the two reactions was 72.5%.

Separation of the Products with Girard Reagent.—The procedure was essentially that of Girard and Sandulesco.[11] The product (10 g.) of the reaction of ethylmagnesium bromide and *trans*-3-hepten-2-one in 30 ml. of absolute ethanol, 3.5 ml. of glacial acetic acid, and 5 g. of Girard reagent (m. p. 176–180°), prepared according to the method given in "Organic Syntheses,"[12] were refluxed on a water-bath for one hour. The mixture was cooled and poured into 250 g. of ice and water containing 2.9 g. of sodium carbonate. The non-ketonic material was separated from this by three extractions with ether and the extracts dried with sodium sulfate. The aqueous layer was treated with 15 ml. of concentrated hydrochloric acid and allowed to stand for one hour at room temperature, during which time the ketonic condensation product was hydrolyzed. The ketone was then removed by extraction three times with ether and the ether extracts dried with sodium sulfate. The ether solution in each case was transferred to a tared distilling flask and the ether removed under reduced pressure at room temperature. During the last fifteen minutes of the distillation, the flask was surrounded by a water-bath kept at 30°. The weight of each residue was accurately determined.

The same procedure was followed with the products of the reactions of the isopropyl and *t*-butyl Grignard reagents. In some cases, 20-g. samples were taken for analysis, and in all cases a 10–15% excess of Girard reagent was used.

4-Ethyl-2-heptanone.—The ketonic product from the reaction of ethylmagnesium bromide was distilled under reduced pressure. It distilled constantly at 75° at 20 mm., and was saturated to bromine and 2% potassium permanganate solution. The semicarbazone, prepared by the method of Eccott and Linstead[2] and recrystallized from dilute ethanol, melted at 116–117°. Colonge[5] gave a b. p. of 72° at 12 mm. for this ketone and the m. p. of the semicarbazone as 115°. The 2,4-dinitrophenylhydrazone, recrystallized from 95% alcohol, melted at 47–48°.

Anal. Calcd. for $C_{15}H_{22}O_4N_4$: N, 17.39. Found: N, 17.42.

4-Isopropyl-2-heptanone.—The ketonic product from the reaction of isopropylmagnesium bromide was distilled under reduced pressure; b. p. 82–84° at 14 mm. It was saturated to bromine and neutral permanganate solution. The semicarbazone, prepared as above, melted at 148–149°.

Anal. Calcd. for $C_{11}H_{23}ON_3$: N, 19.71. Found: N, 19.90.

The 2,4-dinitrophenylhydrazone, recrystallized from 95% alcohol, melted at 60–61°.

Anal. Calcd. for $C_{16}H_{24}O_4N_4$: N, 16.66. Found: N, 16.57.

4-*t*-Butyl-2-heptanone.—The ketonic product from the reaction of *t*-butylmagnesium chloride was distilled under reduced pressure; b. p. 90–95° at 14 mm. It was saturated to bromine and neutral permanganate solution. The semicarbazone, prepared as above, melted at 157.5°.

Anal. Calcd. for $C_{12}H_{25}ON_3$: N, 18.49. Found: N, 18.32.

The 2,4-dinitrophenylhydrazone, recrystallized from 95% alcohol, melted at 65–66°.

Anal. Calcd. for $C_{17}H_{26}O_4N_4$: N, 15.99. Found: N, 15.91.

Summary

1. The *trans* isomer of 3-hepten-2-one has been prepared by a modification of the method of Eccott and Linstead.

2. The reactions of *trans*-3-hepten-2-one with ethyl- and isopropylmagnesium bromides and *t*-butylmagnesium chloride have been studied. The products of 1,2- and 1,4-addition of these Grignard reagents have been separated by means of Girard reagent and the amount of saturated ketone determined.

3. The per cent. of 1,4-addition of the different Grignard reagents to *trans*-3-hepten-2-one is as follows: ethyl, 24.2%; isopropyl, 46.3%; *t*-butyl, 34.9%.

4. This marked increase in the extent of 1,4-addition of the isopropyl Grignard reagent over that of both ethyl and *t*-butyl Grignard reagents has not been noted previously in the results of analogous experiments of other investigators. This indicates that factors other than steric hindrance determine the extent of 1,4-addition to a conjugated carbonyl system.

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(10) Allen, THIS JOURNAL, **52**, 2955 (1930).

(11) Girard and Sandulesco, *Helv. Chim. Acta*, **19**, 1095 (1936).

(12) "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, New York, N. Y., 2nd ed., 1943, p. 85.