[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Δ^2-Cyclohexenone and Related Substances

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In view of the recent paper of Bartlett and Woods,[1] we are presenting the findings of our studies on the preparation and reactions of Δ^2-cyclohexenone and related compounds.

For some time this Laboratory has been interested in the rearrangements accompanying the oxidation of olefins.[2] In connection with this interest, cyclohexene was oxidized with chromic anhydride in acetic acid solution. No evidence of ring contraction or other rearrangement was detected; however, 37% of the cyclohexene attacked was converted to Δ^2-cyclohexenone. The other principal product was adipic acid. Similarly 1-methylcyclohexene was oxidized; 20% of the olefin attacked was found as Δ^1-methylcyclohexene-3-one and 2% as Δ^1-methylcyclohexene-6-one.

Having a convenient method for the preparation in quantity of this interesting alpha,beta-unsaturated ketone it was decided to study its reactions with various Grignard reagents. Kohler[3] made the prediction that the simpler alpha,beta-unsaturated cyclic ketones, because of their highly reactive carbonyl group, would give only 1,2-addition unless the reactivity of the group was diminished by substitution in the alpha position. His work as well as that of others[4] supported this prediction. Contrary to such predictions, the present investigation has shown 1,4-addition with all Grignard reagents studied. It should be noted that much of the early work on this subject was carried out with small amounts of materials so that the presence of minor products might well have been overlooked. A summary of the products obtained with the various Grignard reagents is given in Table I.

TABLE I

	Percentages			
Grignard reagent	1,2-Addition	1,4-Addition	Reduction	Complex products
Methyl	38	15	0	18
Ethyl	52	24	0	13
Isopropyl	10	44	12	16
t-Butyl	0	70	0	14

It will be noted that the relative amounts of 1,2- and 1,4-addition vary considerably with the reagent. In the case of *t*-butylmagnesium chloride no 1,2-addition product could be identified. That *t*-butylmagnesium chloride favors 1,4-addition has recently been shown by the work of Stevens[5] who found that this reagent with crotonic aldehyde gave much better yields of 1,4-addition product than any other reagent tried except *t*-amylmagnesium chloride. The same was found to be the case with 2-pentene-4-one.

Our work confirms the findings of Bartlett and Woods[1] in that Δ^2-cyclohexenone reacts sluggishly with dienes. 1,3-Cyclohexadiene failed to give an adduct after prolonged refluxing. Bartlett and Woods were able to obtain condensation with dienes only from sealed tube reactions. We too obtained Δ^2-cyclohexenol in good yield from the action of aluminum isopropoxide on the ketone.

Preliminary experiments on the action of various Grignard reagents on isophorone, which has a methyl group in the beta position, gave no indication of saturated ketone with methyl or ethyl reagents but gave about 8% saturated ketone with isopropyl Grignard reagent. The results from isophorone are clear enough to indicate that substitution in the 3-position hinders 1,4-addition since with Δ^2-cyclohexenone all four reagents gave some 1,4-addition.

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Experimental

Oxidation of Cyclohexene.—Cyclohexene,[6] b. p. 82° (739 mm.), $n^{20}\text{D}$ 1.4460, 410 g. (5 moles), and 1 kg. of glacial acetic acid were placed in a 5-liter flask equipped with mercury sealed stirrer, reflux condenser, thermometer, and dropping funnel. Over a period of sixteen hours a solution of 750 g. (7.5 moles) of chromic anhydride in a mixture of 450 g. water and 1.5 kg. acetic acid was added with stirring at 25–35°. Stirring was continued for fourteen hours. The product was distilled through a 16-plate column until the temperature reached 98° (742 mm.). After separating the water in the distillate, 181 g. of cyclohexene, $n^{20}\text{D}$ 1.4450, was recovered. The acetic acid in the residue was neutralized about 70% by means of 50% sodium hydroxide. At this point the product had a ten-

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[1] Bartlett and Woods, THIS JOURNAL, **62**, 2933 (1940).

[2] Whitmore and co-workers, *ibid.*, **56**, 1128 (1934).

[3] Kohler, *Am. Chem. J.*, **36**, 181 (1906); **37**, 369 (1907).

[4] Bamberger and Blangley, *Ber.*, **36**, 1625 (1903); Auwers and Keil, *ibid.*, **36**, 1861 (1903); Auwers and Peters, *ibid.*, **43**, 3087 (1910); Mazurewitsch, *J. Russ. Phys.-Chem. Soc.*, **43**, 980 (1911); *Chem. Zentr.*, **82**, II, 1922 (1911).

[5] Stevens, THIS JOURNAL, **57**, 1112 (1935).

[6] "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, New York, N. Y., 1932, p. 177.

dency to become gelatinous. The mixture was then extracted several times with ether. On distilling off the ether, Δ^2-cyclohexenone, 99 g., 37% yield based on the cyclohexene attacked, b. p. 67° (25 mm.), 166° (734 mm.), $n^{20}{\rm D}$ 1.4879, d^{20} 0.9962, was obtained. Only a little acetic acid was obtained on distillation indicating that most of it was tied up in basic chromium salts. The water layer from the above extraction was completely neutralized and the chromium precipitate filtered off. The filter cake was slurried in boiling water and filtered, this process being repeated two times. The combined filtrates, about 25 liters, were evaporated to dryness. The residue was divided in two equal parts and one part acidified with 50% sulfuric acid followed by the addition of 1 liter of ethanol to precipitate sodium sulfate which was then filtered off. The water and alcohol were then evaporated and the residue diluted with water and continuously extracted with ether for two days. On evaporation of the ether, 42 g. of adipic acid, m. p. and mixed m. p. 152–153°, was obtained. This corresponds to a 25% yield from the cyclohexene attacked. A total of four oxidations of cyclohexene were carried out giving yields of Δ^2-cyclohexenone varying from 33 to 38%.

The identity of the Δ^2-cyclohexenone was established by a number of reactions: semicarbazone, m. p. 167–168°, 2,4-dinitrophenylhydrazone, 116–117°, oxime, 90–91°; treatment with bromine gave tribromophenol, m. p. and mixed m. p. 92°; reduction with aluminum isopropoxide gave a 74% yield of Δ^2-cyclohexenol,[7] 74° (25 mm.), 1.4861, phenylurethan, 105–106°.

Oxidation of 1-Methylcyclohexene.—1-Methylcyclohexanol was prepared by the action of methylmagnesium bromide on cyclohexanone. This alcohol was dehydrated with iodine to give 1-methylcyclohexene. In the manner described above, 140 g. (1.45 moles) of the hydrocarbon, 107° (733 mm.), 1.4500, in 470 g. of acetic acid was oxidized with 230 g. (2.3 moles) of chromic anhydride in 140 g. of water and 470 g. of acetic acid. On working up as above, a 20% yield, calculated on the reacted olefin, of Δ^1-methylcyclohexene-3-one, 24 g., 76–78° (14 mm.), 1.4934–1.4938, semicarbazone, 200–201° dec.,[8] 2,4-dinitrophenylhydrazone, 175–176°,[9] and a 2% yield of Δ^1-methylcyclohexene-6-one,[10] 2.5 g., 172–176° (738 mm.), 1.4803, oxime, 61–62°, semicarbazone, 207–208° dec., were obtained.

The Action of Δ^2-Cyclohexenone and 1,3-Cyclohexadiene.—A solution of 30 g. of Δ^2-cyclohexanone in 60 g. of 1,3-cyclohexadiene,[11] 79° (738 mm.), 1.4737, was allowed to stand for three days at room temperature. There was no change in color and the $n^{20}{\rm D}$ only changed from 1.4765 to 1.4768 indicating no reaction. The solution was then refluxed on the steam-bath for twenty-two hours to give a slight yellow coloration and an index of 1.4779. Fractionation of the product gave an almost quantitative recovery of the starting materials. The residue, 4.5 g., was of a rubbery nature and was not identified. Indications were that it was a polymer and not an adduct.

The Addition of Δ^2-Cyclohexenone to Methylmagnesium Bromide.—The Grignard reagent obtained by bubbling methyl bromide (Dow) into 300 ml. of dry ether in which was suspended 24.3 g. (1 mole) of magnesium was cooled to −5° and a solution of 48 g. (0.5 mole) of Δ^2-cyclohexenone in 300 ml. of dry ether added during two hours. The addition was carried out below 0° with vigorous stirring. After standing overnight the product was decomposed by pouring into 1 kg. of ice and 250 g. of ammonium chloride. The ether layer was separated and the water extracted with more ether and the combined extracts dried over sodium sulfate. The ether was distilled off through a 5 plate column. The residue was shaken up with 300 ml. of saturated sodium bisulfite solution to yield a white bisulfite addition compound. The product was filtered off and washed with ether and the filtrate extracted with ether. The addition of more bisulfite solution gave no precipitate. Addition of 100 g. of sodium bicarbonate in 300 ml. of water to the bisulfite addition compound, followed by steam distillation, liberated the ketone. The ketone was fractionated through a 15 plate column to give only material of b. p. 163° (730 mm.), $n^{20}{\rm D}$ 1.4456–9, semicarbazone, 181–182°, 2,4-dinitrophenylhydrazone, 157–158°. All fractions were saturated to bromine. The constants and derivatives check those of *i*-3-methylcyclohexanone.[12] The amount of material, 8 g., represents a 15% yield. The ether extract from the filtrate of the addition complex was dried and fractionated through the 15-plate column to give material of b. p. 63–65° (20 mm.), 1.4732–40, d^{20} 0.9512, which was unsaturated to bromine and alkaline permanganate. Attempts to prepare a phenylurethan resulted only in dehydration. The properties and method of preparation indicate that it is 1-methyl-Δ^2-cyclohexenol from 1,2-addition of the Grignard. The yield was 38%; mol. ref., calcd. 33.39; found 33.13. The suspected carbinol, 15 g., was dehydrated by distilling at atmospheric pressure with 0.1 g. of anhydrous copper sulfate. The water obtained, 2.3 g., represented a 95% dehydration. The oil layer, 10 g., was dried and fractionated to give material, 106.5–107° (738 mm.), 1.4793–1.4806. This compound was very unsaturated; oxidation with potassium permanganate gave a 24% yield of succinic acid, m. p. and mixed m. p. 188–189°; mixing with maleic anhydride in thiophene-free benzene gave a crystalline adduct, m. p. 65–66°.

The high boiling material from the reaction of methylmagnesium bromide and Δ^2-cyclohexenone appeared to be a complex condensation product which was not identified.

Addition of Δ^2-Cyclohexenone to Ethylmagnesium Bromide.—To 1 mole of ethylmagnesium bromide in 300 ml. of solution was added 48 g. (0.5 mole) of Δ^2-cyclohexenone in 200 ml. of ether at 0° during three hours with vigorous stirring. After standing for nine hours the product was worked up as above to give 15.2 g., 24%, of 3-ethylcyclohexanone, 190° (732 mm.), 1.4518, semicarbazone, 182–183°, *p*-nitrophenylhydrazone, 129–130°, 2,4-dinitrophenylhydrazone, 146–147°. These constants and derivatives check with those of v. Braun.[13] A 52% yield of unsaturated material, 74–76° (20 mm.), 1.4770–65,

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(7) Guillemonat, *Compt. rend.*, **205**, 67 (1937).

(8) Simonsen and Storey, *J. Chem. Soc.*, **95**, 2112 (1909); Vorländer and Gartner, *Ann.*, **304**, 23 (1899).

(9) Marvel and Levesque, THIS JOURNAL, **60**, 280 (1938).

(10) Urion, *Compt. rend.*, **199**, 363 (1934).

(11) Hofmann and Damm, *Mitt. schles. Kohlenforsch. Inst. Kaiser-Wilhelm-Ges.*, **2**, 97 (1925); *C. A.*, **22**, 1249 (1928).

(12) Signaigo and Cramer, THIS JOURNAL, **55**, 3326 (1933).

(13) Von Braun, Mannes and Reuter, *Ber.*, **66B**, 1499 (1933).

d^{20} 0.9439, was also obtained. This material dehydrated in attempts to prepare a phenylurethan. This proved it not to be the reduction product. Dehydration with copper sulfate gave impure material which had the odor of ethylbenzene but which also reacted with maleic anhydride. A 97% yield of water was obtained. The tertiary alcohol had a molecular refraction of 37.76; calcd. 38.01. High boiling material, 13%, which appeared to be condensation products was obtained from the above reaction.

Addition of Δ^2-Cyclohexenone to Isopropylmagnesium Chloride.—To 1 mole of isopropylmagnesium chloride in 300 ml. of solution was added 48 g. (0.5 mole) of Δ^2-cyclohexenone in 200 ml. of dry ether over a period of two hours at 0°. The product was worked up as before. Δ^2-Cyclohexenol, 65–67° (13 mm.), 1.4852–3, phenylurethan, m. p. and mixed m. p. 105–106°, was obtained in 12% yield. An unsaturated tertiary alcohol, 6.6 g., 72–74° (13 mm.), 1.4788, 10% calculated as 1-isopropyl-Δ^2-cyclohexenol was isolated but the small amount of material prevented positive identification. This compound dehydrated when treated with phenyl isocyanate. The residue amounted to 16%. 3-Isopropylcyclohexanone, 31 g., 205° (736 mm.), 1.4562–3, semicarbazone, 189–190°, 2,4-dinitrophenylhydrazone, 139–140°, was found in 44% yield. These values check those of Crossley and Pratt.[14] The ketone was saturated to bromine and alkaline permanganate.

Addition of Δ^2-Cyclohexenone to *t*-Butylmagnesium Chloride.—To 1 mole of *t*-butylmagnesium chloride in 300 ml. of solution was added 48 g. (0.5 mole) of Δ^2-cyclohexenone in 300 ml. of dry ether over a period of two hours at 0° with vigorous stirring. After standing overnight, the product was decomposed and worked up as above. Unchanged Δ^2-cyclohexanone, 10%, was recovered. A 70% yield of a saturated ketone, 96–98° (20 mm.), 220° (736 mm.), 1.4615, d^{20} 0.9177; mol. ref., calcd. for 3-*t*-butylcyclohexanone 46.29; found 46.09; semicarbazone, 207–208° dec., 2,4-dinitrophenylhydrazone, 158–159°, was obtained. From its properties and method of preparation this must be 3-*t*-butylcyclohexenone. Intermediate cuts, 2.1 g., which would have contained the reduction product Δ^2-cyclohexenol were dehydrated when treated with phenyl isocyanate. This was probably due to small amounts of tertiary alcohol from 1,2-addition. The high boiling residues amounted to 14%.

Preliminary Experiments on the Action of Grignard Reagents on Isophorone.—In the manner described above 1.5 moles of isophorone was treated with 2 moles of methylmagnesium bromide to give an 83% yield of an unsaturated tertiary alcohol, m. p. 37–38°, believed to be 3,3,5,5-tetramethyl-Δ^2-cyclohexenol; 10% of the isophorone was recovered unchanged. The reaction of isophorone with ethylmagnesium bromide gave an 80% yield of an unsaturated tertiary alcohol, m. p. 49–50°, presumably 1-ethyl-3,5,5-trimethyl-Δ^2-cyclohexenol; 10% of the isophorone was again recovered. The reaction with isopropylmagnesium bromide gave an 8% yield of a saturated ketone, 115° (20 mm.), 1.4657, 2,4-dinitrophenylhydrazone, m. p. 154–155°, semicarbazone, 199–200° dec.; this compound was probably 3-isopropyl-3,5,5-trimethylcyclohexanone.

Summary

1. The oxidation of cyclohexene with chromic anhydride in acetic acid gave 37% of the cyclohexene attacked as Δ^2-cyclohexenone. 1-Methylcyclohexene, in like manner, gave 20% Δ^1-methylcyclohexene-3-one and 2% Δ^1-methylcyclohexene-6-one.

2. The action of various aliphatic Grignard reagents on Δ^2-cyclohexenone has been studied. Methyl Grignard gave 38% 1,2-addition and 15% 1,4-addition; ethyl gave 52% and 24%; isopropyl gave 10% and 44% and also 12% reduction; *t*-butyl gave no detectable 1,2-addition but gave 70% 1,4-addition.

3. Preliminary experiments with isophorone and various Grignard reagents indicated that the methyl group in the 3-position hinders 1,4-addition. Methyl and ethyl reagents gave no 1,4-addition while isopropyl gave only 8% 1,4-addition.

4. The findings indicate clearly that the relative amounts of 1,2- and 1,4-addition are a function of the Grignard reagent used.

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(14) Crossley and Pratt, *J. Chem. Soc.*, **107**, 175 (1915).