minutes, and a pinch of urea was added to destroy any excess nitrous acid. This solution of the diazonium salt was added with stirring to a cold solution of 12.8 g. (0.13 mole) of freshly prepared cuprous chloride in 120 ml. of concentrated hydrochloric acid, and the resulting mixture was stirred until it reached room temperature and then warmed on a steam-bath for fifteen minutes. It was extracted with three 500-ml. portions of benzene, and the benzene extracts were washed with water, with several portions of 0.25 *N* sodium hydroxide solution, and again with water. The benzene was evaporated and the residue distilled (b.p. 130–150° (1–2 mm.)) to give 14.2 g. (50% yield) of crude 4-chloro-5-methoxyacenaphthene. After several crystallizations from methanol, material melting at 84–86° was obtained.

Anal. Calcd. for $C_{13}H_{11}ClO$: OCH_3, 14.2; Cl, 16.2. Found: OCH_3, 14.0; Cl, 16.1.

B. From 4-Chloro-5-acenaphthenol (V).—A solution of 2.05 g. (0.01 mole) of 4-chloro-5-acenaphthenol and 0.6 g. of sodium hydroxide in 25 ml. of water was treated with dimethyl sulfate at 80° in an atmosphere of nitrogen. A total of 2.86 g. (0.0227 mole) of dimethyl sulfate was added in 1.52, 0.67, and 0.67 g. portions at ten-minute intervals, interspersed with the addition of three 2-ml. portions of 2.5 *N* sodium hydroxide. After an additional twenty minutes at 80°, the reaction mixture was extracted with benzene, and the benzene was washed with water and evaporated. Distillation of the residue gave 1.2 g. (55%) of solid material that melted at 84–86° after crystallization from methanol. A mixed melting point determination with authentic 4-chloro-5-methoxyacenaphthene prepared above showed no depression.

Ether Cleavage of 4-Chloro-5-methoxyacenaphthene (XI).—A mixture of 1 g. of XI, 8 ml. of glacial acetic acid, and 4 ml. of 48% hydrobromic acid was heated under reflux in a nitrogen atmosphere for four hours. It was then poured into 25 ml. of water and extracted with three 25-ml. portions of chloroform. The chloroform extracts were washed with three 25-ml. portions of 0.5 *N* sodium hydroxide and, after acidification, the combined aqueous extracts were re-extracted with three 25-ml. portions of chloroform. After washing with sodium bicarbonate solution and drying, the chloroform was evaporated and the residue sublimed at 80° (0.05 mm.). The sublimate was 5-acenaphthenol (50 mg., 6.5% yield), m.p. 125–126°, no depression on admixture with an authentic sample.

When 1 g. of 4-chloro-5-methoxyacenaphthene was heated with 3 g. of pyridine hydrochloride according to the procedure by Prey,[21] the reaction product, isolated as above, consisted of 230 mg. (30%) of 5-acenaphthenol, m.p. 125–126°.

(21) V. Prey, *Ber.*, **74**, 1219 (1941).

BERKELEY, CALIFORNIA RECEIVED NOVEMBER 4, 1950

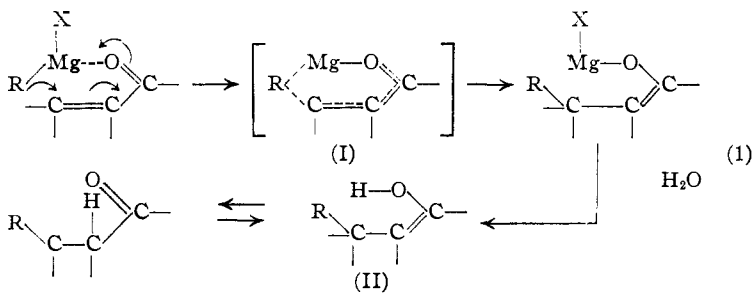
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Studies on the Mechanism of Conjugate Addition. I. The Addition of Grignard Reagents to 2-Cyclohexenone and Some Open Chain Analogs

BY ELLIOT R. ALEXANDER[1] AND GEORGE R. CORAOR

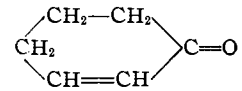
A comparison has been made of the conjugate addition of ethyl, isopropyl and *t*-butyl Grignard reagents to 2-cyclohexenone and its open chain analogs, 3-penten-2-one, 3-hexen-2-one, 3-hepten-2-one and 4-hexen-3-one. Except for the addition of ethylmagnesium bromide, the amount of conjugate addition to 2-cyclohexenone is comparable to the amount of conjugate addition to its open chain analogs. These results suggest that a possible path of reaction involving a cyclic intramolecular transition state is relatively unimportant.

One of the most attractive mechanisms which has been proposed for the conjugate addition of Grignard reagents to α,β-unsaturated ketones[2] involves an intramolecular cyclic transition state (I). It can account for the initial formation of an enol (II) which has been observed in some instances[3] and since lithium alkyls probably do not coördinate



(I) (1)

as readily as Grignard reagents, it provides an explanation for the fact that organolithium reagents give more 1,2-addition than Grignard reagents.[4] It is clear, however, that the cyclic, intramolecular process cannot be the only route leading to conjugate addition, for it has been reported that 2-cyclohexenone (III) undergoes conjugate addition



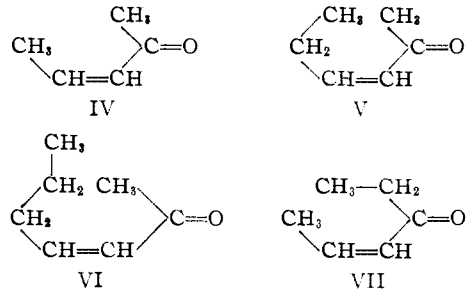
(III)

with Grignard reagents[5] yet the distance between the carbonyl oxygen and the β-carbon atom of this compound appears to be too great to permit the formation of a complex such as I. Accordingly it seemed desirable to compare under conditions as nearly standardized as possible, the addition of Grignard reagents to cyclohexenone and its open chain analogs in order to get a measure of the possible importance of an intramolecular cyclic mechanism in conjugate addition. This paper describes the addition of ethyl, isopropyl and *t*-butyl Grignard reagents to 2-cyclohexenone (III), 3-penten-2-one (IV), 3-hexen-2-one (V), 3-hepten-2-one (VI) and 4-hexen-3-one (VII).

Experimental[6]

2-Cyclohexenone.—This compound was prepared by the thermal dehydration of 2-hydroxycyclohexanone.[7] In a representative run 180 g. (1.6 moles) of 2-hydroxycyclo-

(1) Deceased October 23, 1950.
(2) R. E. Lutz and W. G. Reveley, THIS JOURNAL, **63**, 3184 (1941).
(3) E. P. Kohler, *Am. Chem. J.*, **38**, 181 (1906).
(4) H. Gilman and R. H. Kirby, THIS JOURNAL, **63**, 2946 (1941).
(5) F. C. Whitmore and G. W. Pedlow, *ibid.*, **63**, 758 (1941).
(6) All boiling points and melting points are uncorrected.
(7) P. D. Bartlett and G. F. Woods, THIS JOURNAL, **62**, 2933 (1940).



IV V

VI VII

hexanone gave 42 g. (43%) of 2-cyclohexenone, b.p. 63–64° (13 mm.), $n^{20}D$ 1.4883.

3-Penten-2-one.—The procedure used for this preparation was that of Grignard and Fluchaire[8] modified to the extent that anhydrous potassium acid sulfate rather than oxalic acid was employed as the dehydrating agent. Thus the product obtained from 150 g. (3.4 moles) of acetaldehyde, 400 g. (6.8 moles) of acetone, 150 g. of ether and 100 ml. of 12% aqueous sodium hydroxide was distilled from 15 g. of anhydrous potassium acid sulfate. After drying the distillate over anhydrous potassium carbonate, redistillation through a 16-in. column packed with glass helices gave 84 g. (29%) of 3-penten-2-one, b.p. 121–122°, $n^{20}D$ 1.4377.

3-Hexen-2-one.—This ketone was prepared by the modified method of Grignard and Fluchaire described above. From 200 g. (3.4 moles) of propionaldehyde was obtained 111 g. (24%) of 3-hexen-2-one as a slightly yellow oil, b.p. 64–70° (57 mm.), $n^{20}D$ 1.4423.

3-Hepten-2-one.—After several exploratory experiments the procedure of Eccott and Linstead[9] was adopted. Thus from 318 g. (2.4 moles) of 4-hydroxyheptan-2-one [b.p. 91–95° (25 mm.), $n^{20}D$ 1.4354] and 100 g. of anhydrous potassium acid sulfate was obtained, after distillation through 16-in. column packed with glass helices, 162 g. (59%) of 3-hepten-2-one, b.p. 61° (18 mm.), $n^{20}D$ 1.4430.

4-Hexen-3-one.—For this material the method of Blaise[10] as modified by Coates and Cook[11] was employed. It consists in the reaction of finely divided zinc, allyl bromide and propionitrile followed by isomerization of the resulting 5-hexen-3-one with sulfuric acid. The maximum yield of eight runs carried out in this way was 34% based on propionitrile. The final distillation was carried out through a 63-plate "Heligrid" Podbielniak column giving 4-hexen-3-one as a water-white liquid, b.p. 137°, $n^{20}D$ 1.4385.

Grignard Reactions.—Each conjugated, unsaturated ketone prepared was allowed to react with ethylmagnesium bromide, isopropylmagnesium bromide and *t*-butylmagnesium chloride under conditions as nearly identical as possible. The procedure followed was adapted from that used by Smith, Chase and Rhodes[12] and by Whitmore and Pedlow.[5] Since attention to detail is necessary for these and future comparisons, the method is described below with 3-hepten-2-one and ethylmagnesium bromide.

A solution of 56 g. (0.5 mole) of 3-hepten-2-one in 200 ml. of dry ether was added over the course of three hours to a vigorously stirred Grignard reagent[13] prepared from 24.2 g. (1.0 g. atom) of magnesium turnings and 109 g. (1.0 mole) of ethyl bromide in 300 ml.[14] of dry ether. Throughout addition, the temperature of the reaction mixture was maintained at 0–5° by means of an ice–bath. Stirring was continued for one hour after addition was complete and the reaction mixture was allowed to stand overnight at room temperature. The mixture was hydrolyzed by pouring it onto 1 kg. of crushed ice mixed with 250 g. of ammonium chloride. The ether layer was separated, and the aqueous portion extracted with three 100-ml. portions of ether. These extracts and the ether solution were combined and dried overnight with anhydrous magnesium sulfate. The ether solution was then transferred to a tared flask immersed in an ice-bath and the ether was removed under reduced pressure (15–20 mm.) through a 16-in. column packed with glass helices. Evaporation was continued until the residue reached constant weight[15] for 30 minutes. In all cases the weight of the residue was 86–100%.

Analysis.—In order to determine the per cent. conjugate addition in the reaction products, the carbonyl content of the residues was determined by the method of Bryant and Smith.[16] This was assumed to represent the saturated ketone present and the per cent. 1,2-addition was then calculated by difference.

It is evident that for this method to be accurate it had to be demonstrated that no unchanged starting ketone, nor retrograde aldol products obtainable from it were present in the residue obtained after treatment with the Grignard reagents. Accordingly, to test for the presence of hydrolyzed starting ketone, each Grignard reaction product was tested with the fuchsin–aldehyde reagent[17] and Benedict solution. A negative test for aldehydes was found for each of the runs shown in Table I. To test for any unchanged

TABLE I

CONJUGATE ADDITION TO α,β-UNSATURATED KETONES

Results of earlier workers and analytical methods used in brackets.

Ketone	Per cent. conjugate addition from CH_3CH_2MgBr	$(CH_3)_2CHMgBr$	$(CH_3)_3CMgCl$
3-Penten-2-one	53.1, 52.2, 52.0 [0 fractionation][18] [75 oxidation][19]	65.3, 65.6	62.9, 60.5
3-Hexen-2-one	43.9, 42.3	56.6, 56.3	47.2, 48.8
3-Hepten-2-one	52.1, 51.9 [0 fractionation][20] [40 semicarbazone][21] [24 Girard reag.][12]	63.3, 62.7 [46 Girard reag.][12]	60.8, 58.9 [35 Girard reag.][12] 66.3, 66.2
4-Hexen-3-one	68.0, 67.3	80.3, 80.1	66.3, 66.2
2-Cyclohexenone	22.8, 22.7 [24 bisulfite][5]	64.3, 64.7 [44 bisulfite][5]	61.6, 61.5 [70 bisulfite][5]

(8) V. Grignard and M. Fluchaire, *Ann. chim.*, **9**, 11 (1928).

(9) E. N. Eccott and R. P. Linstead, *J. Chem. Soc.*, 905 (1930).

(10) E. E. Blaise, *Bull. soc. chim.*, **33**, 41 (1905).

(11) R. R. Coates and S. W. Cook, *J. Chem. Soc.*, 561 (1942).

(12) M. E. Smith, B. Chase and R. Rhodes, THIS JOURNAL, **66**, 1547 (1944).

(13) M. S. Kharasch and P. O. Tawney [*ibid.*, **63**, 2308 (1941)] have shown that the per cent. conjugate addition to α,β-unsaturated ketones is affected by the presence of metallic magnesium. Accordingly, before each addition, the Grignard solution was inspected carefully to be sure no traces of unreacted magnesium were present. Additional small amounts of the halide were added if necessary.

(14) In the preparation of *t*-butylmagnesium chloride 500 ml. of ether was used.

(15) The removal of ether from the reaction products was carried out with care. If the last traces of ether were not removed, the observed per cent. of saturated ketone would be lower than the actual value, since the composition determined directly (the per cent. conjugate addition—Table I) was based upon the weight of this residue. The per cent. 1,2-addition was calculated by difference (see the next section).

(16) W. M. D. Bryant and D. M. Smith, THIS JOURNAL, **57**, 57 (1935).

(17) R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1948, p. 101.

(18) A. Gry, *Bull. soc. chim.*, **3**, 377 (1908).

(19) E. P. Kohler, *Am. Chem. J.*, **38**, 511 (1907).

(20) V. Grignard and M. Dubien, *Ann. chim.*, **2**, 282 (1924).

(21) J. Colonge, *Bull. soc. chim.*, [5] **3**, 413, 547 (1936).

unsaturated ketone, the ketonic portion of an aliquot of each reaction product was separated from the unsaturated alcohol by the use of Girard reagent (T)[12] and tested with 2% aqueous potassium permanganate. None of the ketonic portions so obtained gave positive tests. All of the unsaturated ketones employed did so immediately.

Discussion

In Table I are summarized the results of our experiments along with those of earlier investigators for comparison. It can be seen that except for the addition of ethylmagnesium bromide, the amount of conjugate addition to 2-cyclohexenone is comparable to the amount of conjugate addition to its open chain analogs. Since a cyclic intramolecular transition state (equation 1) is impossible for 2-cyclohexenone, these results imply that if one possible path for conjugate addition involves such an intermediate, the path is of relatively little importance with the compounds studied. The significance of the relatively low value with ethylmagnesium bromide and 2-cyclohexenone is not yet clear.

There is considerable disagreement among previous workers as to the amount of conjugate addition a given ketone undergoes. The analytical procedures which yielded these widely divergent values were investigated in connection with this study. It was found that fractionation[18,20] is unsatisfactory because of the tendency of the carbinols to dehydrate. Girard reagent[12] proved not to be quantitative; the separated non-ketonic portion gave a positive test with 2,4-dinitrophenylhydrazine.[22] The sodium bisulfite method[5] gave results which agree reasonably well with those obtained by the method of Bryant and Smith.[16] The bisulfite method, however, involves a large number of manipulations and it is limited to those ketones which will form bisulfite addition compounds. The method of Bryant and Smith was found to be the most accurate (±2%), the simplest and the most general of those yet reported.

(22) One other reason that our results differ so much from those which were determined by the use of Girard reagent is that the earlier workers apparently used too little reagent. Thus from 10 g. of the product obtained from the reaction of ispropylmagnesium bromide and 3-hepten-2-one there was separated 4.63 g. (0.03 mole) of saturated ketone. This is all that could have been separated with the 5 g. (0.03 mole) of Girard reagent used. A similar situation appears to have been true in the analysis of the product from ethylmagnesium bromide and 3-hepten-2-one.

URBANA, ILL. RECEIVED NOVEMBER 10, 1950

[CONTRIBUTION FROM THE WEIZMANN INSTITUTE OF SCIENCE]

The Action of *t*-Butyl Hypochlorite on Organic Compounds. III. Phenols[1]

BY DAVID GINSBURG

The action of *t*-butyl hypochlorite on a series of phenols is reported. In most cases, chlorine enters the nucleus ortho to the phenolic hydroxyl group. Possible mechanisms of the reaction are discussed.

In continuation of previous experiments, the action of *t*-butyl hypochlorite on phenols was investigated. According to a brief report by Clark[2] this reagent acts on phenols with almost explosive violence, necessitating the use of diluents to moderate the reaction. Even so, the yields in many cases leave much to be desired, and mixtures of mono- and poly-chlorinated derivatives are often obtained, involving inevitable losses in the course of separation. Therefore, in contradistinction to aromatic aldehydes, the chlorination of phenols with *t*-butyl hypochlorite is not always worthwhile from the preparative point of view. Nevertheless, in certain cases the yields are high and compounds can easily be prepared which are not accessible by other chlorination methods.[3]

With one apparent exception (thymol), *t*-butyl hypochlorite introduces the chlorine atom *ortho* to the hydroxyl group of monohydric phenols. Thus, phenol gives *o*-chlorophenol, and *o*-chlorophenol yields 2,6-dichlorophenol, when treated with one mole of *t*-butyl hypochlorite. Clark's statement[2] that dichlorination of phenol leads to the 2,4-dichloro derivative, could not be substantiated. Also, when dichloro-substitution takes place with mono-*o*-substituted phenols, one of the chlorine atoms enters the free ortho-, the other the para position. In the heretofore unknown dichloro derivative, obtained from carvacrol, the ortho position of one of the chlorine atoms was proven by infrared analysis.

In the case of guaiacol, the para-directing influence of the methoxyl group outweighs the ortho-directing influence of the phenolic hydroxyl group, and 5-chloro-2-methoxyphenol results. Similar effects have been observed in the chlorination of aromatic aldehydes with *t*-butyl hypochlorite.[1]

As in the aldehyde series, nitro groups deactivate the ring: *o*- and *p*-nitrophenols do not react. The previously noted[1,2] deactivating effect of the carboxyl group is outweighed by the activating influence of the hydroxyl group: salicylic acid is attacked ortho to the phenolic group, yielding 3-chloro-2-hydroxybenzoic acid[2] (see also Table I).

The chlorination of *o*-cresol with *t*-butyl hypochlorite gave a mono- and a dichlorinated product. The latter was the known 4,6-dichloro-2-methylphenol, the former, therefore, presumably either 4- or 6-chloro-2-methylphenol. As its condensation product with chloroacetic acid was not identical with Synerholm and Zimmerman's[4] 4-chloro-2-methylphenoxyacetic acid (m.p. 119–120°), it must have been the 6-chloro-isomer[5] and the monochlorinated *o*-cresol, 6-chloro-2-methylphenol.

(1) Paper II in this series: D. Ginsburg, THIS JOURNAL, **73**, 702 (1951).

(2) B. F. Clark, *Chem. News*, **143**, 265 (1931).

(3) For example, treatment of phenol with chlorine gives mainly *p*-chlorophenol, with *t*-butyl hypochlorite the *o*-isomer.[1]

(4) M. E. Synerholm and P. W. Zimmerman, *Contrib. Boyce Thompson Inst.*, **14**, 91 (1945); *C. A.*, **40**, 1473 (1946).

(5) It proved identical with the product obtained by Haskelberg (*J. Org. Chem.*, **12**, 426 (1947)) upon chlorination of 2-methylphenoxyacetic acid.