BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 40 174—177 (1967)

The Reaction of Cyclooctatetraene Oxide with Grignard Reagents

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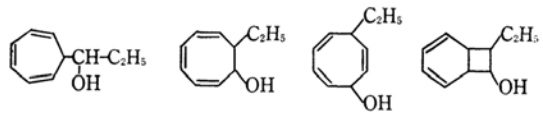
(Received May 17, 1966)

The reaction of cyclooctatetraene oxide with ethylmagnesium bromide, phenylmagnesium bromide and *t*-butylmagnesium bromide was found to yield 2, 4, 6-cycloheptatrienyl-1-ethyl-, phenyl- and *t*-butylcarbinol respectively. The treatment of cyclooctatetraene oxide with a catalytic amount of magnesium bromide in ether afforded phenyl acetaldehyde in a 76% yield. The dehydration of the carbinols with a catalytic amount of *p*-toluenesulfonic acid resulted in their further rearrangement to *trans*-β-substituted styrenes.

There have been several previous papers indicating the facile isomerization of cyclooctatetraene oxide (I) in reactions with cationic reagents[1-4] or in the Diels-Alder reaction.[5] Moreover, Büchi and Burgess[6] have recently reported the formation of isomeric cycloheptatrienecarboxyaldehydes by thermal rearrangement. However, no behavior of I in reaction to any anionic reagent has yet been investigated except the isomerization to 2, 4, 6-cyclooctatrienone with strong bases.[7] In our series of studies of the reactions of cyclooctatriene derivatives with organometallic reagents, we found that I reacted with Grignard reagents in anhydrous ether to yield unsaturated carbinols. Ethylmagnesium bromide, phenylmagnesium bromide and *t*-butylmagnesium bromide gave the corresponding unsaturated carbinols in yields of 83%, 73% and 23% respectively. As will be described below, both the physical and the chemical properties of the products appeared to be incompatible with those of the expected cyclooctatrientyl compounds, and further structural studies of the carbinols indicated that the reactions took place with a skeletal rearrangement. In this paper the determination of the structures and some reactions of the carbinols will be described.

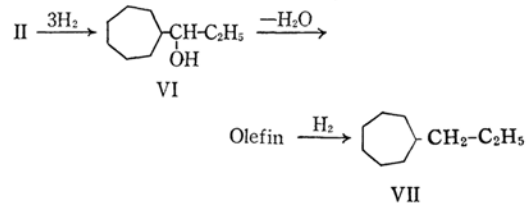
Results and Discussion

Structures of the Unsaturated Carbinols. The viscous oil (II), bp 111.8—112.2°C/18 mmHg, obtained from ethylmagnesium bromide and I showed an ultraviolet absorption at 259 mμ; log ε 3.56 in absolute ethyl alcohol. Upon catalytic hydrogenation in ethyl alcohol with Raney nickel, II absorbed 98.5% of three molar equivalents of hydrogen to yield saturated carbinol (VI). The results indicated the presence of three double bonds conjugated with each other, and they exclude the structures, IV and V, of the possible structures shown below:



II III IV V

Saturated hydrocarbon (VII), obtained by the reactions shown in the following scheme, was proved to be different from ethyl cyclooctane by a study of its infrared spectrum and its refractive index, but the refractive index, n_D^{25} 1.4498, was quite close to that of *n*-propylcycloheptane, n_D^{20} 1.4500, reported by Khromov *et al.*[8]



VI

VII

Although the possibility of rearrangement of the ring in the dehydration step can not be excluded rigorously, the results suggest that VI has a seven-membered ring. VI was, therefore, identified as cycloheptyl ethylcarbinol by a comparison of its

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1) W. Reppe, O. Schlichting, K. Klager and T. Toepel, *Ann.*, **560**, 1 (1948).

2) A. C. Cope, N. A. Nelson and D. S. Smith, *J. Am. Chem. Soc.*, **76**, 1100 (1954).

3) C. R. Ganellin and R. Pettit, *Ber.*, **90**, 2951 (1957).

4) C. R. Ganellin and R. Pettit, *J. Chem. Soc.*, **1958**, 576.

5) A. C. Cope and W. J. Keller, *J. Am. Chem. Soc.*, **80**, 5505 (1958).

6) B. Büchi and E. M. Burgess, *ibid.*, **84**, 3104 (1962).

7) A. C. Cope and B. D. Tiffany, *ibid.*, **73**, 4158 (1951).

8) S. K. Khromov, E. S. Balenkova, P. A. Akishin and B. A. Kazanskii, *Zhur. Obshchei Khim.*, **24**, 1360 (1954); *Chem. Abstr.*, **49**, 21318 (1955).

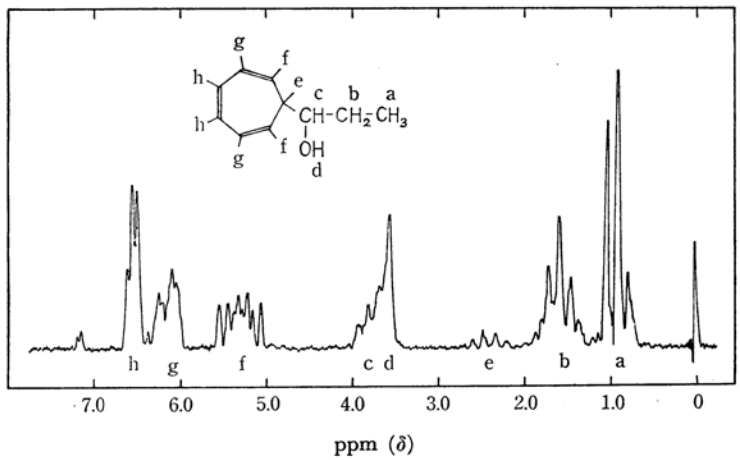
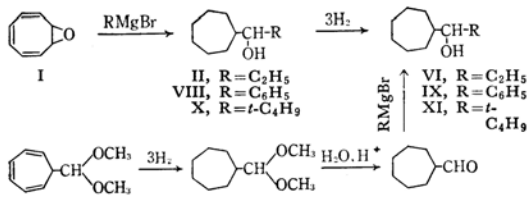


Fig. 1. NMR spectrum of 2,4,6-cycloheptatrienyl ethylcarbinol.

infrared spectrum and the physical constants with those of an authentic specimen,[2] and a mixed-melting-point determination of the α-naphthylurethanes of the two samples was undepressed. Thus we may conclude that the reaction of I with ethylmagnesium bromide does not yield the normal reaction product, 2-ethylcyclooctatrienol (III), but rather, affords the compound with a cycloheptatrienyl ring.

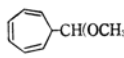
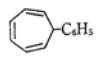
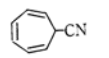
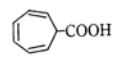
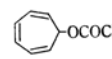


The solid substance (VIII) obtained from phenylmagnesium bromide and I gave white needles on recrystallization from *n*-hexane, mp 83.5°C λ_{max} 259 mμ; log ε 3.58. A small amount of *trans*-stilbene, mp 124—125°C, was obtained as a by-product in the separation of VIII from the reaction mixture by vacuum distillation. The hydrogenation of VIII gave a saturated carbinol (IX), which was identified as cycloheptyl phenylcarbinol by a study of its infrared spectrum and a mixed-melting-point determination with α-naphthylurethane.

The reaction of I with *t*-butylmagnesium bromide also gave cycloheptatrienyl *t*-butylcarbinol (X), bp 97.5—99.0°C/6.5 mmHg, λ_{max} 254 mμ: log ε 3.81, in a poor yield with a large amount of resinous compounds and a small amount of β-*t*-butylstyrene. The strong absorption in the 700—750 cm^{-1} region which is characteristic of the cycloheptatrienyl ring[9] was found in the infrared spectra of all the unsaturated carbinols.

The results showed that the products are cycloheptatrienyl alkyl- and arylcarbinols, but the positions of three double bonds and substituents in the seven-membered ring remained uncertain. A survey of the literature[10-14] indicated that 1-substituted 2, 4, 6-cycloheptatrienyl compounds show one ultraviolet absorption in the 250—260 mμ region, while other double bond isomers usually

Table 1. Ultraviolet absorption maxima of the products and other 1-substituted 2,4,6-cycloheptatrienyl compounds

Compound		λ_{max}, mμ	log ε	Solvent
II		259	3.51	EtOH
VIII		259	3.58	EtOH
X		254	3.81	EtOH
	[2]	258.5	3.71	cyclohexane
	[10]	256	3.56	a
	[11]	255	3.54	EtOH
	[12]	255	3.54	EtOH
	[14]	256	3.73	isooctane

a Solvent was not indicated.

9) K. Conrow, *J. Am. Chem. Soc.*, **81**, 5461 (1959).

10) W. von E. Doering and L. H. Knox, *ibid.*, **76**, 3203 (1954).
11) W. von E. Doering and L. H. Knox, *ibid.*, **79**, 352 (1957).
12) M. J. B. Dewar, C. R. Ganellin and R. Pettit, *J. Chem. Soc.*, **1958**, 55.
13) K. Weiss and S. M. Lalande, C. S. J., *J. Am. Chem. Soc.*, **82**, 3117 (1960).
14) C. M. Orlando, Jr., and K. Weiss, *J. Org. Chem.*, **27**, 4714 (1962).

have two absorption maxima at shorter and longer wavelengths. The close similarity between the ultraviolet maxima and intensities of II, VIII and X and those of other typical 2, 4, 6-cycloheptatrienyl compounds, shown in Table 1, supports the identification of the structure as 2, 4, 6-cycloheptatrienyl-1-alkyl- and arylcarbinols. The NMR spectrum of II (ppm relative to tetramethylsilane) showed signals (relative areas in parentheses) at 6.54 (2.0), 6.16 (2.0), 5.25 (2.1), 3.68 and 3.56 (2.0), 2.32 (0.9), 1.58 (2.2) and 0.88 (3.0), and could be assigned as in Fig. 1. The chemical shifts of olefin protons, which are quite close to those of cycloheptatriene,[15] and the relative areas are consistent with the proposed structure.

The Reaction of I with Diethylmagnesium and Magnesium Bromide. The ring contraction of cycloalkene oxides in the Grignard reaction has been frequently observed,[16] and it has been proved that magnesium halide in the reaction mixture is responsible for the rearrangement and that dialkylmagnesiums give normal addition products. In order to avoid the effect of magnesium bromide, I was allowed to react with diethylmagnesium, but the only product isolated other than the starting material was cycloheptatrienyl ethylcarbinol. On the other hand, the reaction of I with magnesium bromide in ether was carried out in order to examine the effect of magnesium bromide and in order to get cycloheptatrienecarboxyaldehyde. However, an equimolar amount of magnesium bromide caused the formation of a large amount of resinous compounds and a trace of phenyl acetaldehyde, while with a catalytic amount of magnesium bromide, phenyl acetaldehyde was obtained in a yield of 76%.

Some Reactions of Cycloheptatrienyl Carbinols. The removal of one molecule of water from the unsaturated carbinols was expected to afford interesting heptafulvene derivatives. However, the dehydration of the carbinols by a catalytic amount of iodine or *p*-toluenesulfonic acid was found to cause a further rearrangement, yielding aromatic compounds. Thus, cycloheptatrienyl ethyl- and phenylcarbinols gave *trans*-β-ethylstyrene and *trans*-stilbene respectively. Many attempts were made to obtain ketones by the oxidation of the unsaturated carbinols, but no isolable products other than small amounts of benzaldehyde and benzoic acid resulted.

Experimental

Cycloheptatrienyl Ethylcarbinol (II). Twelve grams of I (bp 65—66°C/8 mmHg; n_D^{25} 1.5381; prepared from cyclooctatetraene by epoxidation with monoperphthalic acid) in 20 m*l* of ether was added under nitrogen to a stirred solution of ethylmagnesium bromide (prepared from 3.0 g of magnesium and 13.0 g of ethyl bromide in 120 m*l* of ether); the mixture was then refluxed for one hour. The reaction mixture was cooled with ice water and hydrolyzed with a saturated ammonium chloride solution. The aqueous layer was extracted with three 50-m*l* portions of ether, and the combined ethereal solution was washed with water and dried over anhydrous sodium sulfate. After the ether had been removed, the residue was distilled to give II (12.5 g (83%)), bp 111.8—112.2°C/18 mmHg; n_D^{25} 1.5250; λ_{max} 259 mμ; log ε 3.51. The characteristic absorption assigned to the 2, 4, 6-cycloheptatrienyl ring was found at 705 cm^{-1}. A mixture of 0.4995 g of II and 50 m*l* of ethyl alcohol was hydrogenated with Raney nickel to absorb 246 m*l* of hydrogen (98.5% of three molar equivalents). Seven grams of II in 150 m*l* of ethyl alcohol were hydrogenated; the distillation of the reaction mixture gave 6.5 g of cycloheptyl ethylcarbinol (VI), bp 113.0—113.8°C/20 mmHg; n_D^{25} 1.4736; α-naphthylurethane; the melting point of 77.5—78.0°C was not depressed on admixture with an authentic sample.

Found: C, 77.27; H, 8.26; N, 4.29%. Calcd for $C_{21}H_{27}NO_2$: C, 77.50; H, 8.36; N, 4.30%.

***n*-Propylcycloheptane.** A mixture of 6.5 g of VI and 0.2 g of iodine was placed in a distilling flask equipped with a short column and heated so as to keep the distillation slow. The distillate was then treated in a similar manner with 0.2 g of iodine, and the product was mixed with 80 m*l* of ether. The ethereal solution was washed with a 10% sodium thiosulfate solution and with water, and then dried over anhydrous sodium sulfate. The evaporation of the ether from the dried solution and the distillation of the residue gave; fraction A (3.8 g), bp 68.8—69.1°C/19 mmHg; n_D^{25} 1.4634, and VI, bp 111.0—113.0°C/19 mmHg. Fraction A (0.785 g) in 50 m*l* of ethyl alcohol was hydrogenated with Raney nickel to absorb 141 m*l* of hydrogen (99.1% of one molar equivalent). The reaction mixture was mixed with 100 m*l* of ether, washed thoroughly with water, and dried. The evaporation of the solvent and the distillation of the residue afforded 0.5 g of *n*-propylcycloheptane, bp 70.5°C/21 mmHg, n_D^{25} 1.4498, lit.,[8] n_D^{20} 1.4500. Ethyl cyclooctane was prepared from cyclooctanone: bp 71.0°C/21 mmHg; n_D^{25} 1.4570; lit.,[17] n_D^{25} 1.4568.

Cycloheptatrienyl Phenylcarbinol (VIII) and Cycloheptatrienyl *t*-Butylcarbinol (X). To a stirred solution of phenylmagnesium bromide (prepared from 3.0 g of magnesium and 18.8 g of bromobenzene), 12 g of I in 50 m*l* of ether was added under nitrogen; the mixture was then refluxed for one hour. The reaction mixture was hydrolyzed with a saturated ammonium chloride solution. The aqueous layer was extracted with two 50-m*l* portions of ether, and the combined ethereal solution was washed with water and dried. The evaporation of the solvent afforded a pale yellow solid which, on two recrystallizations from *n*-hexane, gave white needles of VIII, 14.5 g (73%); mp 83.5°C; λ_{max} 259 mμ; log ε 3.58; the characteristic absorption was at 710 cm.

15) "High Resolution NMR Spectra Catalog," Vol. I, Spectrum No. 158, Varian Associates, 1962.
16) N. G. Gaylord and E. J. Becker, *Chem. Revs.*, **49**, 413 (1951).
17) A. C. Cope and H. O. Van Orden, *J. Am. Chem. Soc.*, **74**, 175 (1952).

Found: C, 84.70; H, 7.15%. Calcd for $C_{14}H_{14}O$: C, 84.79; H, 7.11%.

In another run, after the evaporation of the solvent from the dried ethereal solution, the residue was vacuum-distilled to give 13.0 g of a crude product, bp 156.3—162.8°C/12 mmHg. The distillate was dissolved in 150 m*l* of hot methyl alcohol and let stand overnight. The precipitate formed was collected and recrystallized from methyl alcohol to afford 1.0 g of *trans*-stilbene, mp 124.0—124.5°C (*meso*-dibromostilbene, mp 236—236.5°C). Methyl alcohol was evaporated from the filtrate, and the residue gave 10.2 g of VIII on two recrystallizations from *n*-hexane, mp 82.5—83.5°C. VIII (1.5 g) was hydrogenated with Raney nickel in 70 m*l* of ethyl alcohol; the dehydration and reduction which followed yielded 1.2 g of cycloheptyl phenylcarbinol (IX), bp 149.0—149.5°C/10 mmHg; n_D^{25} 1.5445; α-naphthylurethane: mp 51.5—52.0°C.

I (10.5 g) in 50 m*l* of ether was added to a stirred solution of *t*-butylmagnesium bromide (prepared from 3.2 g of magnesium and 18 g of *t*-butyl bromide), and the mixture was refluxed for one hour. After the reaction mixture had been treated as has been described above, distillation yielded an aromatic hydrocarbon which was characterized as β-*t*-butylstyrene by a study of its infrared and ultraviolet spectra (0.5 g); bp 85.0—87.0°C/7 mmHg; n_D^{25} 1.5240, and cycloheptatrienyl *t*-butylcarbinol (X) (3.5 g (23%)); bp 97.5—99.0°C/7 mmHg; n_D^{25} 1.5186; λ_{max} 254 mμ; log ε 3.81. The characteristic absorptions were found at 745 and 705 cm^{-1}. The hydrogenation of X (0.5 g) with Raney nickel afforded cycloheptyl *t*-butylcarbinol (XI) (0.4 g); bp 105—108°C/13 mmHg; n_D^{25} 1.4717; α-naphthylurethane; mp 301.5°C.

The Preparation of Authentic Cycloheptyl Alkyl- and Arylcarbinols. Cycloheptanecarboxyaldehyde dimethyl acetal was prepared by the hydrogenation of 2, 4, 6-cycloheptatriene-1-carboxyaldehyde dimethyl acetal (prepared by the method of Cope *et al.*[2]), bp 74.0—75.9°C/9.5 mmHg; n_D^{25} 1.4510; lit.,[2] n_D^{25} 1.4499—1.4508. A mixture of 20.2 g of cycloheptanecarboxy aldehyde dimethylacetal and 150 m*l* of 20% aqueous sulfuric acid was stirred for half an hour at 60°C. The reaction mixture was then extracted with three 60 m*l* portions of ether, and the combined extracts were washed with a 10% sodium carbonate solution and then with water. The ethereal solution was stirred for 5 hr with an excess amount of a 30% sodium hydrogen sulfite solution. The bisulfite adduct was collected and washed thoroughly with ether. The adduct was suspended in 200 m*l* of ether and hydrolyzed with a 30% potassium carbonate solution. The ether layer was separated, the aqueous layer was extracted with two 30 m*l* portions of ether, and the combined ethereal solution was washed with water and dried. The evaporation of the solvent and the distillation of the residue gave 19.0 g of cycloheptanecarboxyaldehyde, bp 45°C/13 mmHg; n_D^{25} 1.4681; semicarbazone: mp 155.0—155.5°C; lit.,[2] mp 155—156.5°C. Gas chromatographic analysis showed that the product was pure.

The reaction of cycloheptanecarboxyaldehyde with ethylmagnesium bromide, phenylmagnesium bromide, and *t*-butylmagnesium bromide in the usual method gave the following cycloheptyl alkyl- and arylcarbinols respectively:

cycloheptyl ethylcarbinol, 78.5%, bp 94.0—94.5°C/12 mmHg, α-naphthylurethane, mp 77.5—78.0°C,
cycloheptyl phenylcarbinol, 72.2%, bp 169—170°C/11 mmHg, α-naphthylurethane, mp 51.3—52.2°C.
cycloheptyl *t*-butylcarbinol, 34.2%, bp 100—101.5°C/11.5 mmHg, and α-naphthylurethane, mp 301.7°C.

The Reaction of I with Diethylmagnesium. To an ethereal solution of ethylmagnesium bromide, prepared from 33.0 g of ethyl bromide and 7.5 g of magnesium in 150 m*l* of ether, 35 g of dioxane was added at 0°C; the mixture was stirred at room temperature for 2 hr and then let stand overnight. The precipitate formed was removed by centrifuge, and the resulting supernatant liquid was examined by the addition of a small amount of dioxane; no precipitate was formed. The solution was transferred into a reaction flask under nitrogen, and 9.0 g of I in 50 m*l* of ether was stirred into the diethylmagnesium solution. The mixture was refluxed for an hour and then hydrolyzed. After the reaction mixture has been treated as has been described above, distillation yielded I (4.5 g); bp 80—82°C/16 mmHg, and cycloheptatrienyl ethylcarbinol (5.0 g (33%)); bp 109.4°C/16 mmHg.

The Reaction of I with Magnesium Bromide. Four grams of I in 20 m*l* of ether was added at 0°C to an ethereal solution of magnesium bromide (prepared from 0.1 g of magnesium and 0.4 g of bromine), and the mixture was refluxed for an hour. The reaction mixture was then washed twice with water and dried over anhydrous sodium sulfate. Distillation gave 3.0 g (76%) of phenyl acetaldehyde, bp 60—62°C/10 mmHg, which was identified by a study of its infrared spectrum and by the formation of its semicarbazone. The use of an equivalent amount of magnesium bromide in the reaction afforded a few drops of phenyl acetaldehyde and a large amount of a resinous residue.

The Dehydration of Cycloheptatrienyl Ethyl- and Phenylcarbinols. A mixture of II (4.8 g) and 0.2 g *p*-toluenesulfonic acid dihydrate was placed in a small Claisen flask and heated so as to keep the distillation of the reaction product slow. The product distilled out at 180—190°C was collected and mixed with 150 m*l* of ether. The ethereal solution was washed twice with water and dried over anhydrous sodium sulfate. After the solvent had been evaporated, the distillation of the residue afforded 3.3 g (78.5%) of aromatic hydrocarbon, bp 79.0—83.0°C/21 mmHg; n_D^{25} 1.4865. Gas chromatographic analysis showed that the product consisted of 97.9% of *trans*-β-ethylstyrene, identified by a comparison of its infrared absorption with that of an authentic sample previously prepared, and 2.1% of an unknown hydrocarbon.

A mixture of 4.0 g of VIII, 3.0 of phthalic anhydride, and 0.2 g of *p*-toluenesulfonic acid dihydrate in 70 m*l* of benzene was refluxed for an hour. The phthalic acid formed was filtered off, and the filtrate was washed with a 5% sodium carbonate solution and with water and dried. After the benzene had been evaporated, the residue was recrystallized from ethyl alcohol to give white needles (1.0 g; 37.5%) of *trans*-stilbene, mp 124—124.5°C, *meso*-dibromostilbene, mp 236—236.5°C.