change (final value 1.4004). Fractionation of the isomerized product gave 4.9 liters (3316 g. 80% yield) of 2-methyl-2-pentene, which was acetylated in the same manner as above, except that the acetylated product was steam distilled without treatment with $NaHCO_3$. Fractionating the acetylation products, 1760 g., gave 350 g. of recovered olefin (most of the recovered olefin was separated during the steam distillation); 566 g. ketonic material, b. p. 60–64° (40 mm.), $n^{20}\text{D}$ 1.4113–1.4284; 571 g. of 3-ethyl-4-methyl-4-pentene-2-one,[10] b. p. 64.5° at 48 mm., $n^{20}\text{D}$ 1.4285–1.4287 and 500 g. of higher boiling material (residue). The unsaturated ketone was hydrogenated over copper chromite and fractionated (510 g.) to give 175 g. of foreshot-containing ketone and 310 g. of 3-ethyl-4-methyl-2-pentanol, b. p. 165°, $n^{20}\text{D}$ 1.4331.

The above alcohol, 310 g., was dehydrated over alumina as previously described, giving 260 g. of olefins which were fractionated to yield 100 g. of 3-ethyl-4-methyl-1-pentene, b. p. 106°, $n^{20}\text{D}$ 1.4095, and 150 g. of 3-ethyl-4-methyl-2-pentene, b. p. 114–115°, $n^{20}\text{D}$ 1.4210–1.4220. Ozonolysis of VIII gave formaldehyde identified as its 2,4-dinitrophenylhydrazone. No derivative was obtained for the other ozonization product, 3-methyl-2-ethylbutanal, which is unknown. Further proof of structure is based on the fact that the accompanying olefinic products agreed with the physical properties reported for 3-ethyl-4-methyl-2-pentene.[11] Also the infrared spectrum of VIII showed it to be a type I olefin.

Discussion

2,4-Dimethyl-3-hexene.—The method chosen for this synthesis was the dehydration of 2,4-dimethyl-3-hexanol since it was desired to obtain more dehydration data on secondary alcohols. The olefins from the alumina dehydration of 2,4-dimethyl-3-hexanol were found to be a mixture of several isomers as expected. The main portion of the mixture was the desired *cis* and *trans* isomers. Thus, as Fig. 1 shows, the dehydration was slightly more to the secondary butyl group than to the isopropyl group.

Secondary alcohols with double branching on the α-carbon give on dehydration, even with the mildest dehydrating agents, large amounts of rearranged products. Thus pinacolyl alcohol gives only rearranged products with the more acid catalyst and 40% rearranged products over alumina.[12] Secondary alcohols with no α-branching in general give no detectable rearrangement over alumina.[13] However, the dehydration of a secondary alcohol with single branching on the α-carbon leads to rearrangement of the α-hydrogen or alkyl groups in the order of 5%. 2,4-Dimethyl-3-hexanol has branching on both α-carbons and the products from such rearrangements (25%) undoubtedly explain the first and last portions of the curve (Fig. 1).

Summary

The last three of the 66 isomeric octenes have been synthesized, 5,5-dimethyl-2-hexene, 2,4-dimethyl-3-hexene and 3-methyl-4-ethyl-1-pentene. The geometric forms of the first two have also been separated. Three other octenes, 5,5-dimethyl-1-hexene, 2,4-dimethyl-2-hexene, and 3-ethyl-4-methyl-2-pentene (*cis* and *trans*) have also been made in the course of the other preparations. The principal physical properties have been reported on highly purified samples of all the above isomers.

The dehydration of 2,4-dimethyl-3-hexanol has been studied as an example of a secondary alcohol with single branching on both α-carbons. Rearrangements of the order of 25% occurred, most of which resulted in changes of the carbon skeleton.

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(10) The unconjugated double bond position has been assumed from the low refractive index and b. p. as compared with other similar structures that are known.

(11) Reed, Doctor's Dissertation, Ohio State University, 1938.

(12) Whitmore and Meunier, This Journal, **55**, 3721 (1933); Cramer and Glasebrook, *ibid.*, **61**, 230 (1939).

(13) Whitmore and Homeyer, *ibid.*, **55**, 4194 (1933).

State College, Penna. Received June 2, 1949

Contribution from the Whitmore Laboratory of The School of Chemistry and Physics of The Pennsylvania State College]

The Reaction of Mesityl Oxide with *t*-Butylmagnesium Chloride

By Frank C. Whitmore,[1] D. P. J. Goldsmith,[2] N. C. Cook, J. C. Yarze[3] and G. G. Ecke

The addition of mesityl oxide to *t*-amylmagnesium chloride[4] gives a 16% yield of the 1,4-addition product, 4,4,5,5-tetramethyl-2-heptanone. Stevens[5] was unable to obtain the corresponding ketone by addition of mesityl oxide to *t*-butylmagnesium chloride at −10 to −20°. We have now obtained this ketone, 4,4,5,5-tetramethyl-2-hexanone in 3% yield by adding mesityl oxide to *t*-butylmagnesium chloride at 35° in conventional glass equipment and in 6.3% yield in a copper reactor at 15–25°. The ketone was degraded by the haloform reaction to 3,3,4,4-tetramethylpentanoic acid, identical with that obtained by the reaction of carbon dioxide with the Grignard reagent of chlorohexamethylethane.[6] The ketone was also converted into the hydrocarbon 2,2,3,3-tetramethylhexane, identical with a sample previously obtained in this Laboratory.

The other products of the reaction were 20% recovered mesityl oxide, 35% of two unrearranged C_{10} dienes and 1% of rearranged C_{10} diene from the dehydration of 2,2,3,5-tetramethyl-4 or 5-hexen-3-ol, 2% of 2,2,3,5-tetramethyl-4 or 5-hexen-3-ol and 10% of residue. A considerable

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[3] Present address: The M. W. Kellogg Co., Jersey City, N. J.

[4] Whitmore and co-workers, This Journal, **63**, 650 (1941).

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

[6] Whitmore, Marker and Plambeck, *ibid.*, **63**, 1626 (1941).

TABLE I

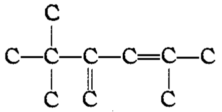
SUMMARY OF PHYSICAL PROPERTIES

Compound	B. p., °C., 760 mm.	d*t*/d*p* at 760 mm.	$n^{20}\text{D}$	d*n*/d*t*	d^{20}_4	d*d*/d*t*	Viscosity in centipoises at		
							20°	30°	40°
2-*t*-Butyl-4-methyl-1,3-pentadiene	145.1	0.051	1.4422	0.00048	0.7640	0.00082	0.856	0.744	0.653
2,4,5,5-Tetramethyl-1,3-hexadiene	148.7	.051	1.4502	.00051	.7727	.00086	0.878	0.755	0.659
4,4,5,5-Tetramethyl-2-hexanone	196.1	.056	1.4420	.00040	.8708	.00077	3.06	2.43	1.98
2,2,3,5-Tetramethyl-4 or 5-hexen-3-ol	180–185		1.451	.00043	.852	.00083	3.2	2.3	1.8

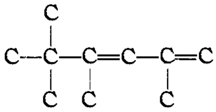
amount of residue, probably condensation products formed from mesityl oxide and the dienes, could not be steam distilled.

It has been noted in this and related work that higher boiling olefins, and especially dienes, cannot always be steam distilled without undesirable effects from the gelatinous basic magnesium halides of the decomposed Grignard complex. Also higher boiling alcohols are often dehydrated, which undoubtedly explains the formation of the dienes since the Grignard complex was not treated with acid.

The structures of the two unrearranged C_{10} diolefins, present in approximately equal amounts, were proven by ozonization



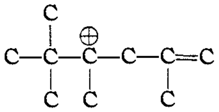
$C-\overset{C}{\underset{C}{C}}-\underset{C}{\underset{\|}{C}}-C=\underset{C}{C}-C$ (I)



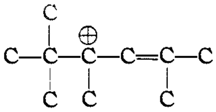
$C-\overset{C}{\underset{C}{C}}-\underset{C}{C}=C-\underset{C}{C}=C$ (II)

B. p. 145.1°, $n^{20}\text{D}$ 1.4422 B. p. 148.7°, $n^{20}\text{D}$ 1.4502

I giving formaldehyde and acetone, and II pinacolone and formaldehyde. The rearranged diene was formed in such small yield (1%) that it was not definitely identified. It appeared to give on hydrogenation 2,3,3,5-tetramethylhexane, the expected structure of a rearrangement. Of the two carbonium ions



$C-\overset{C}{\underset{C}{C}}-\overset{\oplus}{\underset{C}{C}}-C-\underset{C}{C}=C$ (III)



$C-\overset{C}{\underset{C}{C}}-\overset{\oplus}{\underset{C}{C}}-C=\underset{C}{C}-C$ (IV)

it was assumed that III would not rearrange as readily as IV because of the nearness of the double bond, and that the diolefin formed was probably the 1,5- rather than the 1,4-isomer.

The unsaturated alcohol decolorized permanganate and yielded on dehydration water and unsaturated products which boiled in the range of the C_{10} dienes found in the Grignard product. The properties of our alcohol however do not agree with those previously reported[7] from the same reaction by some Russian investigators who appear to have assumed that their reaction product was only 2,2,3,5-tetramethyl-4-hexen-3-ol (b. p. 170–180°, d^{20}_4 0.835, $n^{20}\text{D}$ 1.445; cor. values). Their values seem to be an average arising from a mixture of dienes, alcohol and ketone (Table I). Also the properties of their 2,2,3,5-tetramethylhexane (b. p. 155–165°, d^{20}_4 0.747, $n^{20}\text{D}$ 1.4244; cor. values) derived from their alcohol do not agree with our properties for 2,2,3,5-tetramethylhexane (b. p. 149°, $n^{20}\text{D}$ 1.4147) but again it appears to be a mixture of 2,2,3,5- and 2,2,3,3-tetramethylhexane (b. p. 158°, $n^{20}\text{D}$ 1.4268).

Although we have not located the position of the double bond in the alcohol we are inclined to believe it is in the 5-position. Isomesityl oxide, normally present to about 10% in mesityl oxide,[8] would yield some of the unconjugated isomer which would be more likely to survive dehydration than the conjugated form.

Experimental

First Reaction of Mesityl Oxide and *t*-Butylmagnesium Chloride.—To 8.1 moles of *t*-butylmagnesium chloride in 4500 cc. dry ether, 740 g. (7.5 moles) of mesityl oxide, b. p. 126–127° at 731 mm., $n^{20}\text{D}$ 1.4420, was added during ten hours. After standing overnight the mixture was poured on ice and steam distilled. The distillate was ether extracted and, after removal of the ether, the residue was fractionated. A slight amount of hexamethylethane was obtained, and a 20% yield of a highly unsaturated fraction b. p. 142–144° at 734 mm. This is the dehydration product of 2,4,5,5-tetramethyl-2-hexene-4-ol corresponding to the unsaturated fraction obtained in the addition of mesityl oxide to *t*-amylmagnesium chloride.[4] A 3% yield of 4,4,5,5-tetramethyl-2-hexanone, b. p. 88° at 24 mm., $n^{20}\text{D}$ 1.4418 was obtained, m. p. of 2,4-dinitrophenylhydrazone 138–139°. The ketone was degraded through the haloform reaction to give 3,3,4,4-tetramethylpentanoic acid, m. p. 66–68°, mixed m. p. with known 3,3,4,4-tetramethylpentanoic acid,[6] 67–68°.

Second Reaction of Mesityl Oxide and *t*-Butylmagnesium Chloride.—A larger run (35 moles), similar to the first except that it was made in a 20-l. copper reactor at 15–25°, gave on fractionation in a 35-plate column 20% recovered mesityl oxide; 35% C_{10} dienes, b. p. 145–148°, $n^{20}\text{D}$ 1.4424–1.4500; 1% dienes b. p. 155–160°, $n^{20}\text{D}$ 1.4290–1.4278; 2% 2,2,3,5-tetramethyl-4 or 5-hexene-3-ol, b. p. (145 mm.) 123–129°, $n^{20}\text{D}$ 1.4510; 6.3% 4,4,5,5-tetramethyl-2-hexanone, b. p. (145 mm.) 136°, $n^{20}\text{D}$ 1.4420 and 10% residue.

The principal dienes were separated by refractionation in an 80-plate column at 40 mm. into approximately equal amounts of two isomers 2-*t*-butyl-4-methyl-1,3-pentadiene, b. p. 144.9°, $n^{20}\text{D}$ 1.4422 and 2,4,5,5-tetramethyl-1,3-hexadiene, b. p. 148.5°, $n^{20}\text{D}$ 1.4502. From the ozonolysis of the former was obtained acetone and formaldehyde, and from the latter, pinacolone and formaldehyde, proven by their 2,4-dinitrophenylhydrazones.

A portion of the 4,4,5,5-tetramethyl-2-hexanone was combined with the intermediate boiling at 155–160° and 180–185° (cor. value from b. p. (145 mm.) 123–126°) and hydrogenated (150 ml.). The reduced material was dehydrated over Al_2O_3 at 350°, and the product fractionated through a small 25-plate column; b. p. 144–156°, $n^{20}\text{D}$ 1.4270–1.4395. The main portion of the material boiled at 152–153°, $n^{20}\text{D}$ 1.4370–1.4390° (4,4,5,5-tetramethyl-1-hexene, b. p. 153°, $n^{20}\text{D}$ 1.4370).[9] The olefin mixture (80 ml.) was then hydrogenated and the paraffins frac-

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[7] Petrov, Koptev and Kaplan, *C. A.*, **39**, 1618 (1945).

[8] Stross, Monger and Finch, THIS JOURNAL, **69**, 1627 (1947).

[9] Unpublished work, this Laboratory.

tionated giving a range of material of b. p. 147–155°, n^{20}_D 1.4165–1.4243 (2,2,3,5-tetramethylhexane, b. p. 149°, n^{20}_D 1.4147; 2,3,3,5-tetramethylhexane, b. p. 153°, n^{20}_D 1.4196)[9] and a main portion boiling at 158°, n^{20}_D 1.4265–1.4270 (2,2,3,3-tetramethylhexane, b. p. 158°, n^{20}_D 1.4268).[9]

These data strongly indicate that the intermediate material between the principal dienes and ketone contained 2,3,3,5-tetramethyl-1,5-hexadiene (b. p. 155–160°) and that the 180–185° material was 2,2,3,5-tetramethyl-4 or 5-hexene-3-ol. This latter material also had a strong camphoric odor, split off water when heated with $CuSO_4$ giving lower boiling unsaturated products (b. p. 145–155°), decolorized permanganate, absorbed bromine and gave no derivative with 2,4-dinitrophenylhydrazone. It was present in such small quantities however that it was not obtained in a highly purified state, but undoubtedly contained ketone and dienes.

Physical Properties.—The constants determined for the principal compounds synthesized are given in the accompanying table. The boiling points were measured in a small column-type boiling point apparatus, packed with glass helices and having 3–5 theoretical plates, using thermocouples calibrated to 0.03°. Refractive indices were read on a 5-place Valentine no. 454 refractometer. Densities were measured in pycnometers and viscosities in a modified Oswald viscometer, Cannon Type E.

Summary

On treating *t*-butylmagnesium chloride with mesityl oxide, 6.4% of the reaction product was found to be 4,4,5,5-tetramethyl-2-hexanone, a product of 1,4 addition. Other products of the reaction are: 20% recovered mesityl oxide, 35% of the C_{10} dienes, 2-*t*-butyl-4-methyl-1,3-pentadiene and 2,4,5,5-tetramethyl-1,3-hexadiene, as dehydration products of the normal addition product, 1% of which appeared to be the rearranged C_{10} diene, 2,3,3,5-tetramethyl-1,5-hexadiene, and 1% of 2,2,3,5-tetramethyl-4 or 5-hexene-3-ol. A number of the physical properties of the above compounds have been determined.

STATE COLLEGE, PENNA. RECEIVED JUNE 13, 1949

[CONTRIBUTION FROM THE DOMINION RUBBER COMPANY LIMITED, RESEARCH LABORATORIES]

The Alkaloids of Fumariaceous Plants. XLIII. The Structures of Cularine and of Cularimine

BY RICHARD H. F. MANSKE*

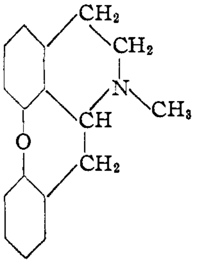
Cularine, $C_{20}H_{23}O_4N$, is an alkaloid which has been isolated from *Corydalis claviculata* and from *Dicentra cucullaria*, *D. eximia*, *D. formosa* and *D. oregana*.[1] It has three methoxyl groups and an indifferent oxygen. Neither oxidation, nor reduction, nor acetylation of the alkaloid yields products which would indicate the presence of alcoholic or ketone groups.

The nitrogen is tertiary and has one methyl group since it is eliminated as trimethylamine in the second step of the Hofmann degradation which also gives rise to a doubly unsaturated compound, $C_{19}H_{18}O_4$, still containing the three methoxyl groups. Cularine on treatment with ethyl chloroformate and alkali yields a compound which is regarded as a urethan, thus indicating the presence of an N-methyltetrahydroisoquinoline nucleus.

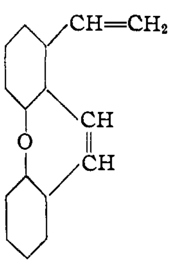
The compound $C_{19}H_{18}O_4$ on oxidation with permanganate yields a tribasic acid, $C_{18}H_{16}O_{10}$, as chief product, and therefore one of the double bonds must be extracyclic and the other in a ring. The loss of only one carbon atom shows that the extracyclic double bond is present as $RCH{=}CH_2$. Such degradations are characteristic of aporphine alkaloids but the above acid still contains the indifferent oxygen and the three methoxyl groups. The only carbon atoms lost are those of the N-methyl group and of the terminal methylene.

Isoquinoline alkaloids containing ether-linked oxygen are generally of the type containing two isoquinoline nuclei and therefore the determination of molecular weights was of some importance but in such types the cryoscopic method of determining them is generally unreliable. Nevertheless the cryoscopic method with camphor gave values which indicated the single molecular formula without question but, more important, the degradation unsaturated compound gave a Rast value of 298 whereas theory demands 310 for the single formula.

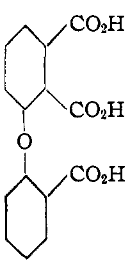
It was therefore obvious that a structure must be written in which there is present a benzylisoquinoline nucleus containing an ether bridge between the two benzene nuclei (I). Such a formula



I



II



III

serves to explain adequately the degradation *via* (II) to the acid (III) (plus three methoxyls in each case). Along with the acid (III) there was always encountered a monobasic acid, $C_{17}H_{14}O_7$, which contained, in addition to the carboxyl and three methoxyls, two extra oxygen atoms. The formation of this acid involved the loss of two

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* Editorial Board 1939–1948.

[1] Manske, *Can. J. Research*, **B16**, 81 (1938).