[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

The Hydroperoxides from *l*-Bornyl Chloride Obtained by Oxidation of the Grignard Reagent[1]

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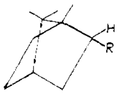
Inverse oxidation of the Grignard reagent from *l*-bornyl chloride gives a mixture of 56% bornyl and 44% isobornyl hydroperoxides in 90% total yield. The same products are obtained from the reagent "isomerized" as described by Riviere,[4] making it doubtful that his product is a single stereoisomer. The hydroperoxides decompose rapidly in boiling benzene to give *l*-camphor and α-*d*-campholenic acid, the latter apparently formed by a polar rearrangement.

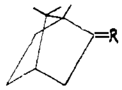
The oxidation of the Grignard reagent derived from bornyl chloride (I) has been investigated by several workers, but with conflicting results. Early studies[2] indicated 65–80% yields of borneol (II). However, Vavon and Berton,[3] working with *l*-bornyl chloride (I) and analyzing their product by optical rotation, found it to be a mixture of 60% *l*-borneol and 40% *d*-isoborneol (VII). The presence of both epimers was also confirmed by separation. When the oxidation was carried out in boiling toluene the sole product was *l*-borneol.

More recently Riviere[4] also has obtained a mixture of epimers (57% *d*-borneol and 43% *l*-isoborneol) from the room temperature oxidation of the Grignard reagent from *d*-bornyl chloride.

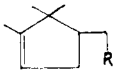


I, R = Cl
II, R = OH
III, R = COOH
IV, R = MgCl
V, R = OOH

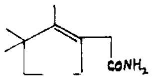
VI, R = Cl
VII, R = OH
VIII, R = COOH
IX, R = MgCl
X, R = OOH



XI, R = O
XII, R = N–OH



XIII, R = CN
XIV, R = COOH
XV, R = $CONH_2$



XVI

Carbonation similarly gave a product which was approximately a 50-50 mixture of *endo*-2-camphanecarboxylic acid (III), [α] +12°, and the *exo* isomer (VIII), [α] −45°. When the Grignard reagent was refluxed in xylene for a few hours, the resulting reagent gave only the *endo*-2-camphanecarboxylic acid when treated with CO_2; however, treatment of this isomerized reagent with oxygen gave the same mixture of borneol and isoborneol as before.

Riviere has proposed that the original reagent obtained from bornyl chloride is a mixture of approximately equal quantities of bornylmagnesium chloride (IV), and isobornylmagnesium chloride (IX). Heating epimerizes the isobornylmagnesium chloride so that the resulting reagent is pure IV, the more stable isomer. As further evidence he has cited the observation that a reagent which is 80–85% isobornylmagnesium chloride can be prepared by treating the mixture with 50% of the theoretical amount of CO_2. The remaining reagent gives 80–85% *exo* acid VIII with CO_2 but when treated with O_2, it gives the same 50-50 mixture of borneol and isoborneol. Unfortunately, the structures of the acids III and VII have not been rigorously established by other methods. These reactions are used as part of their proof of structure.

If Riviere's contention is correct, the isomerized reagent would be the only known example of a Grignard reagent which exists as a single stereoisomer and in which the metal is bonded to an asymmetric carbon atom. Such an organolithium compound has, however, been prepared at low temperatures with partial retention of configuration.[5] Its activity was also established by carbonation.

Since we have found that the oxidation of Grignard reagents can be interrupted at the hydroperoxide stage by adding the reagent to oxygen-saturated solvents at a low temperature[6] we decided to reinvestigate the oxidation to see whether the initial step with the "isomerized" reagent is perhaps stereospecific and to investigate the properties of the unknown bornyl and isobornyl hydroperoxides V and X.

Oxidation of the Grignard reagent from *l*-bornyl chloride[7] by the low temperature inverse technique gave a 90% yield of hydroperoxides, evidently a mixture of V and X, since reduction with NaI in isopropyl alcohol produced a mixture of 56% *l*-borneol and 44% *d*-isoborneol, analyzed by optical rotation.

Oxidation of the Grignard reagent "isomerized" as described by Riviere also gave a 90% yield of hydroperoxide. Attempts to purify the material by recrystallization from petroleum ether, however, yielded a white solid containing only 60% hydroperoxide. Infrared analysis showed that the impurity was chiefly camphor, 38% of this material being present. Presumably, this is formed by the thermal decomposition discussed below. The entire mixture was reduced with $LiAlH_4$ to give a product which was found to be 60% *d*-isoborneol and 40% *l*-borneol from optical rotation. The reduction of camphor by $LiAlH_4$ has been studied and found to give a mixture which is 90% isoborneol and 10% borneol.[8] Therefore, the ratio of isomers may be corrected for the camphor present. This gives a

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[2] P. Barbier and V. Grignard, *Bull. soc. chim.*, [3] **31**, 840 (1904); A. Hesse, *Ber.*, **39**, 1127 (1906); J. Houben, *ibid.*, 1700 (1906).

[3] G. Vavon and A. L. Berton, *Compt. rend.* **175**, 369 (1922).

[4] C. Riviere, *Ann. Chim.*, **1**, 157 (1946).

[5] R. P. Letsinger, THIS JOURNAL, **72**, 4842 (1950).

[6] (a) C. Walling and S. A. Buckler, *ibid.*, **75**, 4372 (1953); (b) *ibid.*, **77**, 6032 (1955).

[7] Since our starting material was *l*-bornyl chloride our products have the opposite optical rotation from those reported by Riviere.[4]

[8] D. S. Noyce and D. B. Denney, THIS JOURNAL, **72**, 5743 (1950).

mixture of 60% *l*-borneol and 40% *d*-isoborneol formed by reduction of the peroxide present in the sample. Thus, the peroxide formed by oxidation is again a mixture of V and X. Even if the camphor present came from the decomposition of one isomer exclusively, this same conclusion could be drawn, although the ratio of isomers would be somewhat changed.

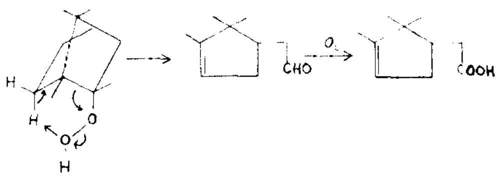
Carbonation of another portion of the same (isomerized) Grignard reagent, however, yielded 78% of *endo*-2-camphanecarboxylic acid (III), [α] −14.95° as the sole isolatable product.

These experiments indicate that Riviere's "isomerized" Grignard reagent does not undergo an initial stereospecific reaction with oxygen, although we confirm the formation of solely the *endo*-acid on carbonation. Since the oxygen reaction is an extremely rapid one[6] occurring at a low temperature, it seems very doubtful that his "isomerized" reagent is actually a single stereoisomer, but rather that the heating and change of solvent in the "isomerization" procedure simply involves some sort of change in the coördination of the Grignard reagent (presumably a complex mixture of ion pairs or partially covalent substances) which causes the carbonation process to follow a preferred stereochemical course.

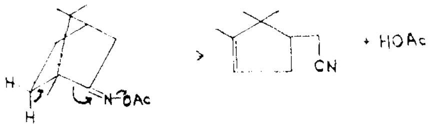
Although we have been unable to separate the bornyl and isobornyl hydroperoxides formed in the oxidation because of their instability, some of the reactions of the mixture are of interest. At 65° in benzene solution they decompose rather rapidly, a 0.69 *M* solution having a half-life of 5 hours. The rate of decomposition with time, followed to about 65% reaction is approximately second order in total peroxide, although the fact that we are dealing with a mixture makes the significance of this observation doubtful.

The products of thermal decomposition were investigated with a larger sample decomposed by refluxing in benzene. Both acidic and neutral products were obtained, but no borneol or isoborneol was formed, since the decomposed material showed no peak in its infrared spectrum at 2.8–3 μ. The neutral fraction proved to be *l*-camphor, corresponding to 60% of the initial peroxide and identified by physical constants, infrared spectrum and as its 2,4-dinitrophenylhydrazone. The acidic fraction was identified as α-*l*-campholenic acid (XIV) by comparison of it and its amide with authentic samples of the *d*-compound prepared from camphor oxime.[9]

l-Camphor is an expected product of the thermal decomposition of the mixture of peroxides by normal radical induced decomposition. The formation of α-campholenic acid is difficult to explain by such a radical decomposition. More plausible is a presumably concerted intramolecular removal of a proton, skeletal rearrangement, and loss of water to give campholenaldehyde which would then rapidly autoxidize in the presence of peroxide to give the observed product. This path would predict that only the endo hydroperoxide (bornyl) would give this product, and resembles the rearrangement of the esters of 9-decalyl hydroperoxide.[10]



The rearrangement is also parallel to that in which camphor oxime (XII) is transformed into campholenonitrile (XIII) by the action of mineral acid or acetyl chloride.[9] The expected path for the rearrangement with the latter reagent would again be a concerted elimination reaction, facilitated in this case by the ejection of a stable acetate anion.



Reaction of the mixture of bornyl and isobornyl hydroperoxides with hot alcoholic KOH was found to give the same products as were obtained by thermal decomposition, *l*-camphor (48%) and α-*l*-campholenic acid (34%). The mixture of hydroperoxides also reacted vigorously with 5% H_2SO_4 in acetic acid. From this, two small liquid fractions were obtained by distillation, but *l*-camphor was the only product which could be identified.

Experimental

Materials.—Our *l*-bornyl chloride was prepared in 60% yield from *l*-α-pinene[11] and anhydrous HCl by the method of Long.[12] It was recrystallized twice from 90% ethanol, m.p. 126–128°, $[\alpha]^{24}D$ −32.8° (ethanol). Prior to preparation of the Grignard reagent *l*-bornyl chloride was dissolved in an equal weight of dry toluene and 25% of the solvent distilled off to remove ethanol and water. The remainder was then used directly in the preparation of the Grignard reagent. The "isomerized" Grignard reagent was prepared as described by Riviere[4] by adding xylene while distilling off ether, and finally boiling the reagent for three hours at 140° under nitrogen.

Oxidations of the Grignard reagent were carried out by inverse addition at −75° essentially as described in our previous paper.[6b] The yields of hydroperoxide, determined by titration, were consistently in the neighborhood of 90%. The composition of the product obtained from the untreated Grignard reagent was investigated in an experiment in which 50 ml. of 0.55 *N* Grignard reagent was added over 43 minutes to an equal volume of oxygen saturated ether at −75°. Following hydrolysis the hydroperoxide could not be extracted from the ether solvent with cold 30% NaOH, so the ether was removed, leaving a pale yellow residue which partially solidified on standing. This residue, which showed a broad peak at 2.8–3 μ in its infrared spectrum characteristic of hydroperoxides, was reduced by dissolving in 45 ml. of absolute isopropyl alcohol, adding 8 g. of NaI and 5 ml. of acetic acid and refluxing 10 minutes. The reaction mixture was poured into water, extracted with ether, and the ether layer decolorized with sodium sulfite solution, dried, and the solvent removed. The residue substantially solidified at −20°, and was pressed dry on a filter to give 1.5 g. of a slightly colored solid, $[\alpha]^{24}D$ −6.2°, corresponding to 56% *l*-borneol and 44% *d*-isoborneol.

Oxidation of the "isomerized" Grignard reagent was carried out with 50 ml. of 1.07 *N* reagent. After hydrolysis the ether and xylene were removed under reduced pressure, taking the bath no higher than 50°, and lowering the pressure finally to 5 mm. An oily yellow solid remained which was recrystallized twice from petroleum ether (30–55°)

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[9] M. A. Behal, *Bull. soc. chim.*, [3] **13**, 834 (1895).

[10] R. Criegee and R. Kaspar, *Ann.*, **560**, 127 (1948); *cf.* P. D. Bartlett and J. L. Kice, THIS JOURNAL, **75**, 5591 (1953).

[11] We are grateful to the Glidden Co., Jacksonville, Florida, for a generous gift of this material.

[12] J. H. Long, THIS JOURNAL, **21**, 637 (1899).

giving 4.65 g. of a white solid, m.p. 109–115°, which contained only 60% of the theoretical amount of peroxide. An infrared spectrum showed a strong carbonyl peak at 5.8 μ. Infrared analysis was performed by taking an initial spectrum of *d*-camphor, and then a spectrum of the mixture using exactly 2.5 times the weight of camphor and made up to the same volume. A value of 38% of camphor was obtained from the intensity of the carbonyl peak, and corroborated by peaks at other wave lengths.

1.30 grams of this mixture was reduced by the method of Russell,[13] by adding the mixture of peroxide and camphor in 20 ml. of ether to 0.98 g. (0.024 mole) of $LiAlH_4$ dissolved in 100 ml. of ice-cold ether and allowing it to stand for 20 minutes. The excess $LiAlH_4$ was decomposed first with ethyl acetate, then water, and the mixture was acidified with HCl. The layers were separated and the ether layer washed with water several times. No peroxide was present. The ether was dried and distilled leaving 1.16 g. (94%) of a white solid which showed an hydroxyl peak in the infrared, but no carbonyl peak. This material had $[\alpha]^{24}D$ +5.6° (ethanol), and is thus a mixture of 60% *d*-isoborneol and 40% *l*-borneol. Correcting for camphor originally present, the peroxide gave a mixture of 60% borneol and 40% isoborneol.

***l*-endo-2-Camphanecarboxylic Acid.**—A sample of the reagent which had been oxidized was carbonated by the method of Hussey[14] to give a 78% yield of carboxylic acid, m.p. 69–71°, after purification by vacuum sublimation, $[\alpha]^{24}D$ −14.95° (toluene); literature for *d*-*endo*-2-camphanecarboxylic acid,[4] m.p. 70 to 86° depending on the crystalline form, and $[\alpha]D$ +12.0° (toluene); reported for the *d*-*exo* isomer $[\alpha]D$ −45.7° (toluene). The acid is thus shown to be *l*-*endo*-2-camphanecarboxylic acid.

Thermal Decomposition of the Mixed Hydroperoxides.—A portion of the residue from a larger scale oxidation containing 7.55 g. (0.0444 mole) of the mixed hydroperoxides was dissolved in 30 ml. of benzene, the mixture refluxed for 19 hours and the bulk of the solvent removed. The residue showed no hydroxyl peak, but had two distinct peaks in the carbonyl region of the infrared. The residue was taken up in 20 ml. of ether and extracted with 20 ml. of 10% NaOH, leaving a neutral layer which was washed with water and subsequently examined.

The basic extracts were neutralized. The yellow oil which separated, combined with further material obtained by ether extraction, yielded finally 2.5 g. of liquid which showed typical carboxyl absorption in the infrared region. A portion was converted to amide with $SOCl_2$ followed by aqueous ammonia. After four recrystallizations from water, using Norite during the first two, white scales of the amide were obtained, m.p. 138–141°. The m.p. reported for α-*d*-campholenamide is 130.5°.[9] *Anal.* Calcd. for $C_{10}H_{17}ON$: C, 71.81; H, 10.25; N, 8.38. Found: C, 71.6; H, 10.4; N, 8.21.

The acid decolorized Br_2 in CCl_4 and dilute $KMnO_4$ solution. The physical properties were $n^{24}D$ 1.4650, $[\alpha]^{24}D$ −8.3° (ethanol). The values reported for α-*d*-campholenic acid are $n^{19}D$ 1.4690, and $[\alpha]D$ +9.37°.[15]

For purposes of comparison, α-*d*-campholenic acid and its amide were prepared by methods described in the literature. The oxime of *d*-camphor was prepared in 97% yield by the method of Auwers,[16] m.p. 117–118°. The oxime was rearranged to the nitrile of campholenic acid, b.p. 97–98° (14 mm.), in 79% yield by boiling with 25% H_2SO_4, according to the directions of Tiemann.[15] α-*d*-Campholenic acid and its amide were obtained by selective basic hydrolysis of the nitrile in 97 and 62% yield, respectively, essentially by the method of Behal.[9] The amide melted at 130.0–130.2° after several recrystallizations from very dilute acetone. The acid boiled at 142–144° (10 mm.), $n^{26}D$ 1.4682.

The infrared spectra of α-*d*-campholenic acid and the acid obtained from the thermal decomposition were identical. Thus, this acid is shown to be α-*l*-campholenic acid. The spectra of the amides were quite similar, but differed slightly at 7.0 and 8.7 μ. From this and the melting point, the amide from the peroxide decomposition may be contaminated by the β isomer formed by isomerization by HCl during the $SOCl_2$ treatment.[9]

The neutral ether layer from the thermal decomposition was distilled until the distillate reached 190°. The residue was vacuum sublimed to give 4.0 g. (60%) of *l*-camphor. This material, after one further sublimation, had m.p. 172–175°, and $[\alpha]^{25}D$ −37.2° (ethanol); literature, m.p. 177.5°, $[\alpha]D$ −42.1°. A 2,4-dinitrophenylhydrazone derivative was prepared, m.p. 168–169°; literature, for *d*-camphor, m.p. 177°.

The rate of thermal decomposition of this mixture of peroxides was studied by heating 25 ml. of a 0.693 molar solution in anhydrous benzene in a thermostat at 65°. One-ml. aliquots were titrated periodically, employing 0.1 *N* sodium thiosulfate. The half-life of the peroxide was 5 hours, and the data, followed to 65% reaction, fitted second-order kinetics.

Reaction of the Hydroperoxides with Base.—9.0 grams of a residue containing 3.80 g. (0.022 mole) of peroxide was heated gently on the steam-bath for 5 hours with 2.5 g. of KOH in 25 ml. of ethanol. The solution was homogeneous throughout. The solution was taken up in 25 ml. of ether and water was added. The layers were separated and the aqueous layer neutralized and extracted with ether. The ether was evaporated and the residue distilled to give 1.30 g. (34%) of α-*l*-campholenic acid, b.p. 147–150° (18 mm.), $n^{19}D$ 1.4703. The infrared spectrum of this material was identical with that of authentic α-*d*-campholenic acid.

The neutral ether layer was distilled until all solvent was removed. The residue was treated with 4.0 g. of 2,4-dinitrophenylhydrazine in acidic aqueous ethanol solution. After standing for several days, the orange precipitate was filtered giving 3.51 g. (48%) of the 2,4-dinitrophenylhydrazone of *l*-camphor. After recrystallization, it melted at 175–176°, and did not depress the m.p. of an authentic sample.

Reaction of the Hydroperoxide with Acid.—17.0 grams of solution containing 6.9 g. (0.040 mole) of peroxide was treated with 25 g. of a 5% solution of H_2SO_4 in acetic acid. After an induction period of about one minute, a vigorous reaction took place and considerable tarry material was formed. The solution was cooled, two volumes of ether added and the mixture washed several times with water. The ether was evaporated and the dark residue distilled to give two small fractions, b.p. 93–97° (18 mm.) and 95–97° (1.5 mm.), the remainder forming a plastic residue. Both fractions showed carbonyl absorption peaks in the infrared and contained *l*-camphor, identified as either its dinitrophenyl hydrazone or semicarbazone.

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[13] G. A. Russell, THIS JOURNAL, **75**, 5011 (1953).

[14] A. S. Hussey, *ibid.*, **73**, 1364 (1951).

[15] F. Tiemann, *Ber.*, **29**, 3007 (1896).

[16] K. Auwers, *ibid.*, **22**, 605 (1889).