Contribution from the George Herbert Jones Laboratory of the University of Chicago

THE DETECTION OF FREE RADICALS IN SOLUTION. IV. THE REACTION OF ALKYL HALIDES WITH SODIUM IN THE PRESENCE OF ISOPRENE

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It has already been demonstrated (1) that a variety of alkyl and aryl halides react with magnesium in the presence of isoprene (and small amounts of ether) to give products of the following types:

 $RX + CH_2 = C(CH_3)CH = CH_2 + Mg \rightarrow R - CH_2 - C = CH - CH_2 - R$ and
(I)

CH₃

$$\begin{array}{cccc} CH_{3} & CH_{2} \\ \downarrow \\ R--CH_{2}-C=CH-CH_{2}-CH_{2}-CH=C-CH_{2}R \\ (+ & some & R--CH_{2}-C=CH-CH_{2}-CH=CH_{2}) \\ & & \downarrow \\ CH_{2}R \end{array}$$
(II)

where R = alkyl or aryl. The total and relative yields of products I and II have been found to depend not only on the nature of the halide but on the experimental conditions of the reaction.

The reaction of *tert*-butyl bromide with sodium in the presence of isoprene has been investigated. Besides compounds I ($R = t-C_4H_9$) (31–33% yield) and II ($R = t-C_4H_9$) (21–32% yield), a small amount (7–8%) of 3,5,5-trimethyl hexene-2 has been obtained. The yields of these last named olefins were not substantially altered when an excess of sodium sand was employed, but substantially larger yields were obtained with sodium dispersions.²

To account for these products the following mechanism is suggested:

1.
$$(CH_3)_3CBr + Na \rightarrow (CH_3)_3C \cdot + NaBr$$

 $CH_3 \qquad CH_3$
2. $(CH_3)_3C \cdot + CH_2 = C - CH = CH_2 \rightarrow (CH_3)_3C - CH_2 - C = CH - CH_2 \cdot (III)$

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 $^{^{2}}$ As yet, no products of the type I or II have been isolated when phenyl bromide, isoprene (and small amounts of ether), and sodium were used, although reasonable yields of these products have been obtained when magnesium (instead of sodium) was used. The results obtained with sodium dispersions (instead of sodium sand) will be reported later.

For simplicity, only one canonical form of III is here indicated (see Ref. 1) and only the products derived from this form are here given.

The reaction products when isoprene and *tert*-butyl bromide react with sodium or magnesium (in the presence of small amounts of ether) are thus the same, except that in the case of sodium some 3, 5, 5-trimethylhexene-2 is also formed. This latter compound could be formed as shown in scheme 3 or *via* one or both of the mechanisms indicated in scheme 6. Furthermore, it may be argued that Compound I ($\mathbf{R} = tert$ -butyl) was formed by the reaction of IV with *tert*-butyl bromide (scheme 6), whereas Compound VII was formed by the reaction of V



with tert-butyl bromide (scheme 7).

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As against the idea that the intermediate organo sodium compounds are solely responsible for products I and II, the following arguments may be cited:

(a) If the reaction mixture contains an intermediate IV (see scheme 6) which (upon hydrolysis) gives the 3,5,5-trimethylhexene-2, then carbonation of the reaction mixture should give rise to acids containing the skeletal structure of IV, in which the sodium atom is replaced by a (COOH) group. No such acids were found, although a search was made for them.

(b) There is even stronger evidence that the "largest amount" of the dimeric material is not formed from organo sodium compounds, as indicated in scheme 7, since Compound VII, although it differs from the Compound II (formed by a free radical mechanism, equations 1–5) only in the position of a methyl group, would not upon ozonolysis give succinic acid. Actually, succinic acid (60%) was isolated when the product was ozonized. This fact lends support to the idea that organo sodium compounds do not participate to an appreciable extent in the formation of Compound II; it favors the free radical mechanism suggested for the formation of this compound.⁴

Little, if any, of the compound, corresponding to A (R = sec-butyl instead of *tert*-butyl), is formed when *sec*-butyl bromide and isoprene react with sodium. Only the Compounds I and II (R = sec-butyl), corresponding to those obtained with magnesium, have been isolated.

³ None of this product was isolated from the reaction mixture, although a search for this material was made.

⁴ Although there is considerable evidence that Compound I is formed by a free radical mechanism, its formation *via* organo-metallic compounds can not be excluded. Additional work is contemplated to evaluate the contribution of these mechanisms in the formation of Compound I and 3,5,5-trimethylhexene-2.

EXPERIMENTAL PART

Reaction between tert-butyl bromide and sodium in the presence of isoprene. To sodium sand (17.6 g.), covered with anhydrous ether (20 ml.), in a 500-ml. three-necked flask equipped with stirrer, dropping-funnel, and reflux condenser, was added dropwise a mixture of tertbutyl bromide (41.1 g.; 0.30 mole) and isoprene (51.0 g.; 0.75 mole).

Reaction commenced readily and was well sustained throughout the addition. When all the reactants had been added, the reaction mixture was heated under reflux with stirring (4 hrs.).

The reaction mixture then was poured onto solid carbon dioxide, and allowed to warm to 0°. Sulphuric acid (5 N, 100 ml.) was added, the organic layer was separated, and the aqueous layer was extracted with ether (3 x 50 ml.). The combined organic extracts then were extracted with 10% sodium carbonate solution (3 x 100 ml.). The alkaline solution was further extracted with 50 ml. of ether and the latter was combined with the main bulk and dried (calcium sulphate).

Acidification of the alkaline solution with hydrochloric acid, extraction with ether $(3 \times 40 \text{ ml.})$, and evaporation of the solvent gave no residue. After continuous extraction of the aqueous portion with ether (5 days), no acidic organic material was obtained.

Ether was removed by careful fractionation from the neutral organic extract, and the residue was fractionated to give the following fractions:

Fraction 1, b.p. 70–73°/750 mm., 3.8 g., n_{μ}^{\pm} 1.4286; Fraction 2, b.p. 32–35°/15 mm., 0.3 g., n_{μ}^{π} 1.4240; Fraction 3, b.p. 35–37°/15 mm., 1.7 g., n_{μ}^{π} 1.4234; Fraction 4, b.p. 40–79°/15 mm., 0.4 g., n_{μ}^{π} 1.4327; Fraction 5, b.p. 79–83°/15 mm., 2.9 g., n_{μ}^{π} 1.4402; Fraction 6, b.p. 83–85°/14 mm., 2.7 g., n_{μ}^{π} 1.4400; Fraction 7, b.p. 84–90°/14 mm., 0.4 g., n_{μ}^{π} 1.4410; Fraction 8, b.p. 92–93°/14 mm., 2.3 g., n_{μ}^{π} 1.4417; Fraction 9, b.p. 78°/1.0 mm.–100°/0.7 mm., 1.2 g., n_{μ}^{π} 1.4528; Fraction 10, b.p. 96°/0.45 mm.–99°/0.4 mm., 11.5 g., n_{μ}^{π} 1.4583.

A cold-trap condensate collected during the water-pump distillation weighed 1.2 g. $(n_p^{23} 1.4225)$.

Fraction 1 was tert-butyl bromide (9%).

Fractions 2 and 3 were 3,5,5-trimethylhexene-2. Yield with redistilled cold-trap condensate = 2.6 g. (7% of calculated amount). Although no formaldehyde was isolated upon ozonolysis of this material, the presence of small amounts of 3,5,5-trimethylhexene-1 can not be excluded.

Molecular weight (fraction 3): Found, 130. C₉H₁₈; Calc'd, 126.

Hydrogenation equivalent: Found, 123.5. C₉H₁₈; Calc'd, 126.

The compound was hydrogenated in glacial acetic acid in the presence of PtO₂. The hydrogenated hydrocarbon boiled at 123°/740 mm. $(n_p^{n.5} 1.4038)$. The recorded constants (2) for 2,2,4-trimethylhexane (C₉H₂₀) are as follows: b.p. 126.7° $(n_p^{20} 1.4034)$.

Anal. Calc'd for C₂H₂₀: C, 85.63; H, 14.37.

Found: C, 85.9; H, 14.1.

Fractions 5-8 were 2, 2, 4, 7, 7-pentamethyloctene-4 (and its isomer). Yield 8.3 g. (30% of calculated amount).

Molecular weight: Fraction 6: Found, 178. C13H26; Calc'd, 182.

Fraction 8: Found, 185. C13H26; Calc'd, 182.

Hydrogenation equivalent: Fraction 5: Found, 172.3. C₁₃H₂₆; Calc'd, 182.

Fraction 8: Found, 180.5. C₁₈H₂₆; Calc'd, 182.

Fraction 9 had a molecular weight of 211 and a hydrogenation equivalent of 137. Thus, it appears to be a mixture of Compound I ($\mathbf{R} = tert$ -butyl) and Compound II ($\mathbf{R} = tert$ -butyl). It does not contain Compound VI, 3,7,9,9-tetramethyldecadiene-2,6 (Calc'd molecular weight 194; hydrogenation equivalent 97).

Fraction 10 was 2,2,4,9,11,11-hexamethyldodecadiene-4,9 (and its isomer) (Compound II, R = tert-butyl). Yield, 11.5 g. (31% of calc'd).

Molecular weight: Found, 253. C18H34; Calc'd, 250.

Hydrogenation equivalent: Found, 126. C₁₈H₃₄; Calc'd, 125.



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Ozonolysis of hydrocarbon C_9H_{18} (Fractions 2 and 3). The hydrocarbon (2.18 g.; 17.3 millimoles), dissolved in dry chloroform (150 ml.) was cooled to 0° and ozonized oxygen (*circa* 0.4 millimoles/min.) was passed in. Ozonolysis was complete in 44 minutes.

The gas, after passing through the sample, was bubbled into a saturated aqueous solution of dimedone. The precipitate which formed was collected and recrystallized twice from aqueous ethanol. It melted at 140–142.5°, and the melting point was not depressed when admixed with an authentic specimen of the dimedone derivative of acetaldehyde.

Chloroform was removed *in vacuo* from the original solution and the residue was treated with water (50 ml.). The mixture was heated under reflux (2 hr.). The oil which separated was extracted with ether, and the aqueous layer was extracted with further quantities of ether (3 x 20 ml.). The combined ethereal extracts were well washed with 10% sodium carbonate solution (3 x 30 ml.). The alkaline extracts yielded no organic material on acidification.

Ether was removed carefully from the neutral product, which on distillation yielded methyl neopentyl ketone (1.0 g.; b.p. 120-125°; n_2^{90} 1.4020). The 2,4-dinitrophenylhydrazone of this ketone, when crystallized from dilute alcohol, melted at 99°.

Moersch and Whitmore (3) report that methyl neopentyl ketone boils at 126° $(n_{p}^{20} 1.4030-1.4036)$.

Ozonolysis of hydrocarbon $C_{18}H_{24}$ (Fraction 10). The hydrocarbon (5.73 g.; 22.9 millimoles), dissolved in dry ethyl acetate (300 ml.), was cooled to -70° and ozonized oxygen (0.5 millimoles/min. was passed. The time of ozonolysis was 96 minutes.

The solvent was removed at reduced pressure and water (100 ml.) was added to the residue. The mixture was heated under reflux (3 hr.) and sodium carbonate solution (100 ml. of 20% solution) was added. The neutral material was extracted with ether (3 x 50 ml.) and the ethereal extracts were washed with further quantities of sodium carbonate solution.

The combined ethereal extract was dried (calcium sulphate) and the solvent was removed by careful fractionation through a helix-packed column. The residue (2.6 g.) on distillation gave methyl neopentyl ketone (b.p. 119-126°, n_n^n 1.4060). The 2,4-dinitrophenylhydrazone of this ketone melted at 98-100°, upon crystallization from dilute alcohol.

The combined alkaline extract was acidified and extracted with ether (50 ml.). Distillation of the ether gave no residue. The aqueous material was extracted continuously with ether (40 hr.). The ether was separated, dried (calcium sulphate), and distilled. The residue (2.5 g.) was semi-solid. After drying at 50° *in vacuo* it solidified completely. The solid was taken up in acetone and recrystallized from acetone. It melted at 179–182° and the melting point was not depressed when mixed with an authentic specimen of succinic acid (1.63 g.; 60% of calculated amount).

Somewhat better conversion of the *tert*-butyl bromide was noted when sodium (dispersed in heptane) was reacted with *tert*-butyl bromide and isoprene.

Reaction of sec-butyl bromide with sodium in the presence of isoprene. Sodium sand (6.9 g.; 0.3 g.-atom) was prepared in a 500-ml. flask equipped with a dropping-funnel, stirrer, and reflux condenser. The sodium was covered with dry ether (20 ml.) and the apparatus was flushed out with nitrogen. A mixture of sec-butyl bromide (41.1 g.; 0.3 mole) and isoprene (51.0 g.; 0.75 mole) was added dropwise to the stirred mixture. The reaction commenced readily and was well sustained throughout the addition. When addition was complete, the reaction mixture was heated under reflux (2 hr.).

Ethanol (50 ml.) was added dropwise and, when the excess of sodium had been destroyed, water (100 ml.) was added. The organic layer was separated and the aqueous layer was extracted with low-boiling light petroleum $(3 \times 40 \text{ ml.})$.

The combined organic material was dried (calcium sulphate) and the solvent was removed by distillation. Unchanged sec-butyl bromide was removed at 25° in vacuo and collected in a cold trap. On distillation the cold trap condensate gave sec-butyl bromide (5.0 g.; 12% recovery) with no higher-boiling material.

The main product was distilled and the following fractions were collected: Fractions 1-3, b.p. $43^{\circ}/0.15 \text{ mm.}-45^{\circ}/0.18 \text{ mm.}, n_{2}^{23}$ 1.4422-1.4431, combined weight 8.4 g.; Fraction 4,

b.p. 61°/0.2 mm.-85°/0.25 mm., n_p^{23} 1.4540, 0.2 g.; Fractions 5 and 6, b.p. 89°/0.35 mm.-102.5°/0.4 mm., n_p^{23} 1.4611-1.4614, combined weight 5.2 g. A cold-trap condensate (0.2 g., n_p^{23} 1.4220) was collected.

Fractions 1-3 were the 2:1 adduct Compound I (R = sec-butyl), substantially 3,5,8-trimethyldecene-6. Yield 8.4 g. (31% of calculated).

Molecular weight (fraction 1): Found, 192. C13H26; Calc'd, 182.

Hydrogenation equivalent (fraction 2): Found, 173. C13H26; Calc'd, 182.

The constants previously obtained for this product (1b) were b.p. $45^{\circ}/0.14$ mm.- $53^{\circ}/0.15$ mm.; n_{ν}^{25} 1.4429-1.4431.

Fractions 5 and 6 were the 2:2 adduct, substantially 3,5,10,12-tetramethyltetradecadiene-5,9. Yield 5.2 g. (14% calc'd).

Molecular weight (fraction 5): Found, 259. C₁₈H₃₄; Calc'd, 250.

Hydrogenation equivalent (fraction 6): Found, 121.7. C18H24; Calc'd, 125.

The constants previously obtained for this product were b.p. $89.5^{\circ}/0.15$ mm.- $105^{\circ}/0.2$ mm.; n_{2}^{25} 1.4606-1.4621.

SUMMARY

1. It has been shown that *tert*-butyl bromide and *sec*-butyl bromide react with sodium (and a dispersion of sodium in a hydrocarbon solvent) in the presence of isoprene to give products similar to those obtained when magnesium is used. A small amount (7-8%) of 3,5,5-trimethylhexene-2, a product not formed when magnesium is used, has also been isolated.

2. With sec-butyl bromide the products obtained by the use of sodium are similar to those when magnesium is used.

3. A mechanism to account for the formation of the products isolated in the reactions described in 1 and 2 above is suggested.

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