

# Synthesis and Transformation of 5- and 2-Methylbicyclo[2.2.1]hept-2-enes and 2-Methylenebicyclo[2.2.1]heptane with Retrospective $\delta$ -Migration of Hydrogen over Oxide Catalyst

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**Abstract**—5- and 2-Methylbicyclo[2.2.1]hept-2-enes and 2-methylenebicyclo[2.2.1]heptane were synthesized by a new procedure, and their transformations in a flow system over stationary layer of aluminosilicate catalyst were studied at various temperatures. At 150–400°C these compounds undergo isomerization which is accompanied by  $\delta$ -migration of hydrogen. The isomerization mechanism is discussed in terms of formation of classical carbocations, not invoking nonclassical carbenium ion.

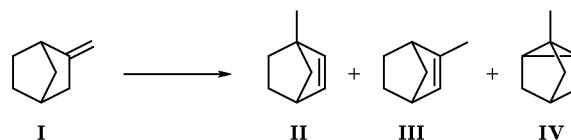
Transformations of hydrocarbons of the bicyclo[2.2.1]hept(en) series were extensively studied in 1960s [1–3]. In the recent years, these compounds attract attention due to efficient biological activity of some substances containing a pharmacophoric norbornene fragment [4–7]. For example, bicyclic neurotropic sulfonamide derivatives possessing analgetic, antiphlogistic, tranquilizing, anticonvulsant, and antihypoxic properties were synthesized [8].

It is known that structural or positional transformations of the bicyclic skeleton occur mainly in the five-membered fragment containing an alkyl group. The alkyl shift in alkylbicycloheptenes is characterized by some specific features. Double bond transfer according to the mechanism typical of alkyl rearrangement in alkenes is hindered (Bredt's rule) [9]; therefore, it involves formation of a nonclassical carbenium ion [10]. Numerous studies have been reported on various transformations of hydrocarbons of the bicyclo[2.2.1]heptene series. However, the mechanism of alkyl group shift or double bond transfer from one ring to the other by the action of protonating agents was usually interpreted in terms of formation of classical and nonclassical carbenium ions.

Among publications on the isomerization of 2-methylenebicyclo[2.2.1]heptane (**I**), the study performed by Blanchard and Germain [1] should be noted. According to the authors, liquid-phase isomerization in the presence of a silicon–phosphorus

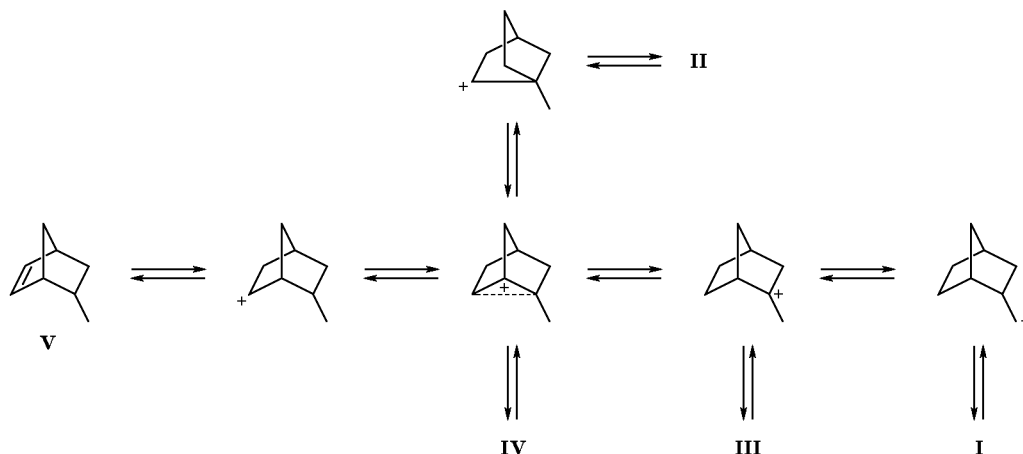
catalyst gives three products: 1-methylbicyclo[2.2.1]hept-2-ene (**II**), 2-methylbicyclo[2.2.1]hept-2-ene (**III**), and 1-methyltricyclo[2.2.1.0<sup>2,6</sup>]heptane (**IV**) (Scheme 1). One more possible isomer, 5-methylnorbornene (**V**), was not detected.

Scheme 1.



A large contribution to the study of transformations of bicyclo[2.2.1]hept(en) derivatives and their mechanism was made by Plate, Belikova, and co-workers [2, 3]. In the isomerization of bicyclo[2.2.1]heptane hydrocarbons over  $\gamma$ -Al<sub>2</sub>O<sub>3</sub>, apart from compound **IV**, the authors detected 3-methylnortricyclene and 4-methylnortricyclene. The double bond migration was accompanied by Wagner–Meerwein rearrangement leading to isomers differing by position of the alkyl group. The isomerization of 5-methylnorbornene (**V**) over SiO<sub>2</sub> afforded products **I–IV** [3] (Scheme 2). Scheme 2 shows all theoretically possible intermediates, both classical and nonclassical carbenium ions, and the corresponding stable compounds. Among the latter, the most difficultly accessible is compound **III** in which the alkyl group is located at the double bond [2, 11].

Scheme 2.

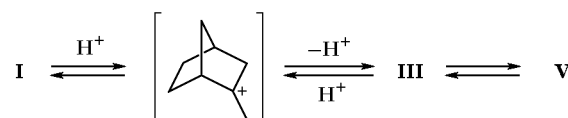


With the goal of developing an efficient procedure for preparation of bicyclo[2.2.1]hept-2-enes having a methyl group at the double bond, we examined thermocatalytic transformations of compound **I**. It was found that the reaction yields 5-methylnorbornene (**V**) via  $\delta$ -migration of hydride ion. Therefore, the catalytic transformation of pure compound **V** was also examined. The results of our systematic studies on the synthesis [12–14] and transformations [15–19] of 5-hydroxymethyl-, 5-methyl-, and 2-methylbicyclo[2.2.1]hept-2-enes and mixtures of methyl-substituted derivatives have already been reported. In the present work, the reactions were carried out in a flow system over a stationary layer of oxide catalysts. The catalytic transformations of pure compounds **I** and **V** were performed under comparable conditions in order to demonstrate retrospective character of  $\delta$ -migration of hydrogen. Compound **I** was synthesized [14] by dehydration of 2-hydroxymethylbicyclo[2.2.1]heptane (**VI**) which was prepared in 74% yield by hydrogenation of 5-hydroxymethylbicyclo[2.2.1]hept-2-ene (**X**) [20] (Table 1).

The results of catalytic transformations of compound **IV** in the presence of  $\gamma$ - $\text{Al}_2\text{O}_3$  and aluminosilicate catalyst in a flow system at a volume rate of

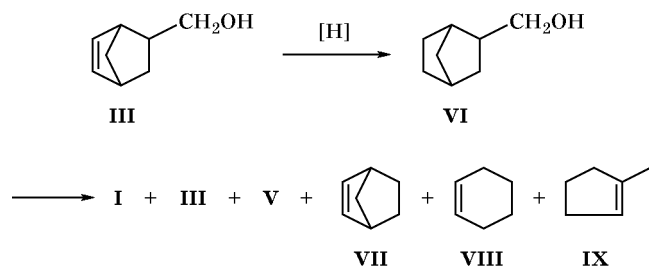
$0.5 \text{ h}^{-1}$  [18] are summarized in Table 1. Depending on the temperature, complex mixtures of compound **I** with methyl-substituted norbornenes and other unsaturated cyclic hydrocarbons are formed as a result of successive transformations (Scheme 3). As follows from the data in Table 1, relatively high acidity of  $\gamma$ - $\text{Al}_2\text{O}_3$  as compared to aluminosilicate favors dehydration of alcohol **VI** at lower temperature, and the yield of compound **I** attains 40% at 200 and  $350^\circ\text{C}$ , respectively.

The formation of a complex mixture of products suggests that compound **I** undergoes further isomerization. Identification of products obtained from pure compound **I** in the temperature range from 150 to  $400^\circ\text{C}$  (Table 2) showed that the isomerization involves  $\gamma$ -migration of hydrogen. Here, 2-methylenebicyclo[2.2.1]heptane (**I**) is converted mainly into 2-methylnorbornene (**III**) which in turn gives rise to 5-methylnorbornene (**V**):



The second stage of the above process is reversible. This was confirmed by the results of catalytic transformation of pure compound **V** under analogous conditions (Table 2). The data in Table 2 show that the major products of methylenebicyclobutane transformation are compounds **III** and **V** when the temperature is not very high. Obviously, in this case  $\delta$ -migration of hydrogen occurs, i.e., the double bond is transferred first into the ring system and then to the  $\delta$ -position with respect to the methylene group. A considerable amount of **III** was also obtained in

Scheme 3.



**Table 1.** Transformation of 2-hydroxymethylbicyclo[2.2.1]heptane over  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> and aluminosilicate catalyst at different temperatures (substrate volume rate 0.5 h<sup>-1</sup>)

Temperature, °C	Product composition, wt %						
	I	III	V <sup>a</sup>	VII	VIII	IX <sup>b</sup>	VI <sup>c</sup>
$\gamma$ -Al <sub>2</sub> O <sub>3</sub>							
200	39.0	1.0	0.5	0.14	0.4	–	59.0
250	39.5	2.1	0.8	0.2	0.4	–	57.0
300	61.4	4.8	1.5	0.4	1.1	–	30.8
350	70.6	5.1	1.5	–	1.3	0.5	21.0
400	47.2	18.7	8.7	–	4.5	13.3	7.6
Aluminosilicate catalyst							
200	1.9	0.6	0.5	Traces	–	–	97.0
250	3.9	0.9	0.6	0.1	0.1	–	94.4
300	15.6	2.6	1.2	0.4	0.4	–	80.0
350	48.8	4.1	1.3	0.3	0.3	0.1	45.3
400	61.0	14.7	4.5	2.5	2.5	6.5	10.8

<sup>a</sup> A mixture of the *endo* and *exo* isomers.<sup>b</sup> Traces of 3- and 4-methylcyclopentenes were also present.<sup>c</sup> Unreacted compound VI.**Table 2.** Transformation of 2-methylenebicyclo[2.2.1]heptane (I) and 5-methylbicyclo[2.2.1]hept-2-ene (V) over  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> and aluminosilicate catalyst at different temperatures (substrate volume rate 0.5 h<sup>-1</sup>)

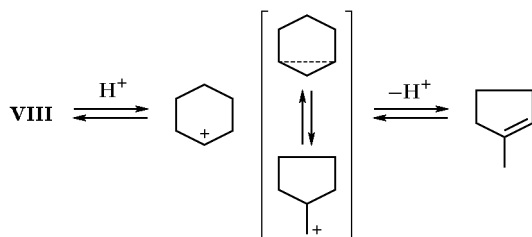
Temperature, °C	I <sup>a</sup>				V <sup>b</sup>				
	III	V	VII	VIII	III	VII	VIII	IX	VI <sup>c</sup>
$\gamma$ -Al <sub>2</sub> O <sub>3</sub>									
150	–	–	–	–	17.1	–	–	–	82.9
200	45.5	53.2	Traces	–	26.7	–	–	–	73.3
250	34.5	47.3	18.2	–	36.6	2.0	1.0	Traces	58.7
300	20.0	62.5	17.5	–	38.6	0.7	0.4	7.2	52.5
350	17.1	62.0	18.2	2.7	36.9	16.0	4.1	7.7	30.3
400	16.4	30.0	30.0	23.6	–	–	–	–	–
Aluminosilicate catalyst									
150	–	–	–	–	8.2	–	–	–	91.0
200	61.7	38.3	–	–	15.7	–	–	–	84.3
250	50.8	49.1	Traces	–	25.5	1.2	0.5	–	72.8
300	34.1	53.7	12.2	–	29.3	1.0	0.8	2.9	66.0
350	36.3	50.0	12.0	1.7	28.1	8.7	2.5	3.8	56.9
400	39.0	27.2	25.8	8.0	–	–	–	–	–

<sup>a</sup> Product composition, wt %, with respect to the reacted compound I.<sup>b</sup> Product composition, wt %, with respect to the initial amount of compound V.<sup>c</sup> Unreacted compound V.

the isomerization of pure 5-methylnorbornene (**V**). Wagner–Meerwein rearrangement, which is intrinsic to bicyclo[2.2.1]hept-2-ene derivatives, either does not occur in a flow system over oxide catalysts or its contribution is so small that the corresponding rearrangement products, 1-methylbicyclo[2.2.1]hept-2-ene (**II**) and methylnortricyclene **IV**, were not detected.

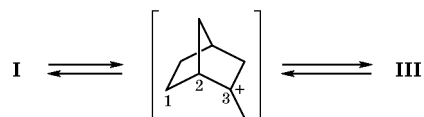
The formation of norbornene may be interpreted in terms of simultaneous demethylation [21] and hydrogenation in the presence of oxide catalyst [22], while cyclohexene may be formed as a result of known [23] methylene bridge elimination followed by demethylation and hydrogenation. At high temperature cyclohexene undergoes profound transformation accompanied by ring contraction (Scheme 4).

Scheme 4.



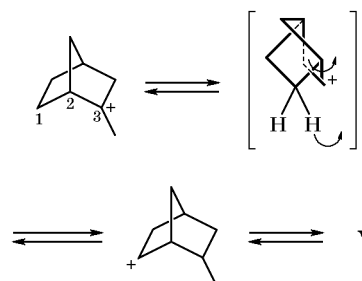
Taking the above stated into account, the isomerization of 2-methylenebicycloheptane (**I**) into norbornenes **III** and **V**, as well as of compound **V** into **III**, can be presumed to involve  $\delta$ -migration of hydride ion, i.e., double bond transfer from one five-membered ring to the other. This process is likely to occur with intermediate formation of only classical carbenium ions with strongly distorted angles between the C–C bonds linking the two rings together (at the bridgehead positions). Depending on the temperature, the isomerization of **I** includes the following steps:

(1) Below 300°C: (a) protonation to give a classical carbocation which is then transformed into compound **III**:



(b)  $\delta$ -Migration of hydrogen due to strong distortion of the C<sup>1</sup>C<sup>2</sup>C<sup>3</sup> bond angle; the distance between the C<sup>1</sup> and C<sup>3</sup> atoms shortens to 1.5 Å, resulting in formation of hydrocarbon **V**. Here, synartetic acceleration due to effect of  $\pi$ -electrons of the semicyclic double bond in molecule **I** cannot be ruled out (Scheme 5).

Scheme 5.



(2) At temperatures exceeding 300°C, the reaction involves rupture of the bridge, demethylation, selective hydrogenation, and skeletal isomerization with ring contraction.

## EXPERIMENTAL

The IR spectra were recorded in the range from 4000 to 700 cm<sup>-1</sup> using a UR-20 spectrophotometer. The <sup>1</sup>H NMR spectra were measured on a Tesla BS-487 instrument (80 MHz) in CCl<sub>4</sub> with TMS as internal reference. The <sup>13</sup>C NMR spectra were obtained on a Varian FT-80 spectrometer at 20 MHz.

The transformations of compounds **I** and **V** were performed in the presence of commercial  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> (A-1) with a specific surface of 200–210 m<sup>2</sup>/g, a bulk weight of 0.5–0.55 kg/l, and a grain size of 3–4 mm and in the presence of an aluminosilicate catalyst having a known composition [21].

Experiments were carried out in a flow setup with a stationary layer of the catalyst in the temperature range from 150 to 400°C. The substrate was supplied at a volume rate of 0.5 h<sup>-1</sup>. The products were identified and quantitated by gas–liquid chromatography on a Tsvet-101 instrument; 3000 × 3-mm column; stationary phase poly(ethylene glycol) adipinate; carrier gas helium (flow rate 40 ml/min), oven temperature 85°C.

Cyclopentadiene was prepared from the dimer [21] and was distilled prior to use, bp 41–42°C,  $d_4^{20} = 0.802$ ,  $n_D^{20} = 1.4445$ .

**2-Methylenebicyclo[2.2.1]heptane (I).** Compound **VI** was subjected to dehydration in a flow system over a stationary layer of  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> at a volume rate of 0.5 h<sup>-1</sup> in the temperature range from 200 to 400°C. A fraction with bp 124–125°C was isolated by distillation. Yield 31–39%,  $d_4^{20} = 0.8801$ ,  $n_D^{20} = 1.4735$ . <sup>13</sup>C NMR spectrum,  $\delta_C$ , ppm (relative to HMDS as internal reference; a mixture of *endo* and *exo* isomers): 44.69 (C<sup>1</sup>), 151.68 (C<sup>2</sup>), 39.54 (C<sup>3</sup>), 36.44 (C<sup>4</sup>), 27.12 (C<sup>5</sup>), 29.85 (C<sup>6</sup>), 40.49 (C<sup>7</sup>), 99.21 (=CH<sub>2</sub>). Found,

%, C 89.02; H 10.98. C<sub>8</sub>H<sub>12</sub>. Calculated, %: C 88.88; H 11.12.

**2-Methylbicyclo[2.2.1]hept-2-ene (III)** [16]. Compound **V** was subjected to isomerization at 200–300°C in a flow system over a natural zeolite, clinoptilolite, containing 70–80% of the crystalline form and having a general formula of (K, Na)<sub>4</sub>Ca(Al<sub>6</sub>Si<sub>30</sub>O<sub>72</sub>)·20H<sub>2</sub>O (14–10% of quartz, 2–2.5% of calcite, 2–2.5 of biotite, and 2–3% of other species). Yield 24.6%, bp 117–120°C,  $d_4^{20} = 0.8608$ ,  $n_D^{20} = 1.4630$ . <sup>13</sup>C NMR spectrum,  $\delta_C$ , ppm: 45.67 (C<sup>1</sup>), 134.05 (C<sup>2</sup>), 125.54 (C<sup>3</sup>), 42.99 (C<sup>4</sup>), 27.12 (C<sup>5</sup>), 24.12 (C<sup>6</sup>), 45.65 (C<sup>7</sup>), 16.32 (CH<sub>3</sub>). Found, %: C 88.25; H 11.75. C<sub>8</sub>H<sub>12</sub>. Calculated, %: C 88.88; H 11.12.

A mixture of methyl-substituted bicyclo[2.2.1]hept-2-enes was obtained in a similar way by isomerization of compound **I** [17].

**5-Methylbicyclo[2.2.1]hept-2-ene (V)** [13]. A mixture of 264 g (4.0 mol) of freshly prepared cyclopentadiene and 369.6 g (8.8 mol) of propene (molar ratio 1:2.2) was heated for 35 min at 200°C in a high-pressure reactor. The adduct was obtained in 93% yield as a mixture of *endo* and *exo* isomers, bp 115–117°C,  $d_4^{20} = 0.8589$ ,  $n_D^{20} = 1.4610$ . <sup>13</sup>C NMR spectrum,  $\delta_C$ , ppm: 39.57 (C<sup>1</sup>), 133.48 (C<sup>2</sup>), 129.31 (C<sup>3</sup>), 41.98 (C<sup>4</sup>), 31.91 (C<sup>5</sup>), 34.31 (C<sup>6</sup>), 47.48 (C<sup>7</sup>), 18.61 (CH<sub>3</sub>). Found, %: C 88.68; H 11.32. C<sub>8</sub>H<sub>12</sub>. Calculated, %: C 88.88; H 11.12.

**2-Hydroxymethylbicyclo[2.2.1]heptane (VI)**. Compound **X**, 186 g (1.5 mol), was subjected to hydrogenation over Ni and Cr<sub>2</sub>O<sub>3</sub> at 200°C in a high-pressure reactor (reaction time 3 h, initial hydrogen pressure 100 atm). Yield 80%, bp 73–75°C (2 mm),  $d_4^{20} = 1.003$ ,  $n_D^{20} = 1.4888$ .

**5-Hydroxymethylbicyclo[2.2.1]hept-2-ene (X)**. A mixture of 300 g (4.5 mol) of freshly prepared cyclopentadiene and 530 g (9.0 mol) of allyl alcohol was heated for 1.5 h at 180°C in a high-pressure reactor. Distillation gave 419 g of adduct **X**,  $d_4^{20} = 1.029$ ,  $n_D^{20} = 1.5008$ . <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.77 (1-H), 5.95 (2-H), 6.07 (3-H), 2.92 (4-H), 2.22 (5-H), 0.45 (*endo*-6-H), 1.77 (*exo*-6-H), 1.45 (*syn*-7-H), 1.24 (*anti*-7-H), 3.1–3.3 (5-CH<sub>2</sub>), 4.18 (OH).

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