INVESTIGATIONS IN THE BICYCLOHEPTANE SERIES PART I. THE ELECTRONIC EFFECT OF METHYL GROUPS ON C₆ OF THE NORBORNYL CATION

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ABSTRACT

The addition of acetic acid to camphenilene has been carried out. The major products are the two expected from normal addition without rearrangement. From the product ratio it is possible to conclude that the difference between the electronic effect of a methyl and a hydrogen at C_6 of the norbornyl cation is small.

Winstein (1-3) and Roberts (4, 5) have proposed that a non-classical carbonium ion (I) is obtained in the norbornyl system by solvolysis of derivatives of *exo*-norborneol. This is analogous to the type of intermediate (II) proposed in a number of migration reactions (6). For many such reactions, i.e. the Baeyer-Villiger and pinacol rearrangement reactions,



a definite order of migrational aptitude of t-butyl > ethyl > methyl has been observed (7, 8) and this order has been partly attributed to electronic influence of the methyl groups on the migrating carbon. It is of interest to see if such pronounced effects are also present in the norbornyl system.

In our laboratories, we are studying the electronic and steric effects of substitution at C_6 of the norbornyl system and in this paper will report evidence concerning the electronic influence of two methyl groups at C_6 .

Addition of acetic acid to camphenilene (apoisofenchene (III)) can potentially yield a simple norbornyl cation (IV) and/or a 6,6-dimethylnorbornyl cation (V) (the non-classical ion is used here for convenience since we do not have definitive evidence for or against its formation). Neglecting any steric differences (which are shown below to be small)



and provided the product is not equilibrated, the product ratio should be a measure of the electronic influence of the methyl groups on the intermediate ion.

Beckmann and Bamberger (9) in 1953 reported the addition of acetic acid to camphenilene. They observed as the major product the acetate from IV (5-exo-camphenilanyl acetate (β -isofenchocamphoryl acetate) (VI)). Two other minor products resulting from

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rearrangement were also found but there was no evidence for the acetate from V (6-exocamphenilanyl acetate) (VII). We now have repeated this work and find that 5-exocamphenilanyl acetate (VI) and 6-exo-camphenilanyl acetate (VII) are the major products and are formed in the ratio of 2:1 respectively.



The acetate mixture from the addition of acetic acid to camphenilene was chromatographed by vapor chromatography and two major peaks were found to be present. These components were isolated and found to be identical with the pair of acetates prepared from camphenilene by the hydroboration method of Brown and Subba Rao (10). Hydroboration of camphenilene followed by oxidation and then acetylation gave two acetates, b.p. 211° and 214°, in a ratio of 45:55 respectively. From studies by Brown *et al.* on bicyclic systems and related structures (11, 12) it is unlikely that rearrangement of the carbon skeleton has occurred and it is probable that the two acetates are *exo.* It is important to note that for a reaction which has been shown to be sensitive to steric effects the ratio of acetates formed is close to 1. It is based on this observation that we feel that steric effects are minor in the addition reaction with acetic acid.

Further identification of the products has been based on the transformation of the acetates to the alcohols and derivatives and then to the ketones and derivatives. The

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pertinent melting points of these and related compounds are given in Table I. From these data it can be concluded that the acetate, b.p. 214°, is 5-exo-camphenilanyl acetate (VI) and the acetate, b.p. 211°, is 6-exo-camphenilanyl acetate (VII).

TABLE I							
	Melting point (°C)						
Source	Alcohol	Hydrogen phthalate	Ketone	Semicarbazone			
<i>i-exo</i> -Camphenilanyl	60-61 (13) 103-104 (15)	130-131(13) 178-170(15)	64-65.5(14)	193(14) 222(16)			
B-Camphenilanyl "2"	75-76 (15)	154-155(15)	38 (16)	223(10) 223(16)			
z-Isofenchocamphoryl	132-133(15)	174-175(15)	109 (17) h p 197 (18)	220 (17)			
Acetate, b.p. 211°	30	138.5 - 140	55–56, b.p. 195	183184			
Acetate, b.p. 214°	55 - 56	130-131		189 - 190			

Beckmann and Bamberger (9) missed the derivatives of the 6-exo-camphenilanyl system for the following reasons. In the attempted separation by crystallization of the hydrogen phthalates of the alcohol mixture the hydrogen phthalate of 6-exo-camphenilanol was

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not obtained since it is more soluble than the 5-isomer in the solvents used. The ketone mixture of 6-camphenilanone and 5-camphenilanone under standard conditions yields the pure semicarbazone of the 5-isomer since the 6-isomer forms a semicarbazone at a much slower rate. The slow reactivity of the 6-ketone is presumably due to the large steric effort of an *endo*-methyl group at the 2-position.

There are two possible explanations for the observed product ratio from the addition of acetic acid to camphenilene. The first is that the presence of methyl substitution at C_6 of I (V) provides no additional stabilization over structure IV and thus the product ratio is close to 1. The ability of methyl attached to the carbon of a migrating group to give stabilization by electronic induction or hyperconjugation has been questioned in the case of the Wagner-Meerwein rearrangement reaction (19). Cram and Knight based their arguments on an observed migrational aptitude for methyl and ethyl of 35:1 respectively in the solvolysis of 3,4-dimethyl-4-phenyl-3-hexyl *p*-bromobenzoate. Unfortunately, there have been no other migrational aptitudes measured for the Wagner-Meerwein rearrangement reaction.

The second possible explanation is that C_6 does not participate during the addition and thus the effect of methyl substitution on C_6 is long range. It is hoped that further studies on the effect of substituents at C_6 of the norbornyl system will provide additional information from which our understanding of the factors involved will be increased.

EXPERIMENTAL

Melting points and boiling points are uncorrected. Boiling points of analytical samples were determined by the micro inverted capillary method.

Camphenilene

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The camphenilene, m.p. $33-34^{\circ}$, b.p. 131° , and n_{D}^{35} 1.4525, used in this study was prepared by methods similar to those reported by Berson (20).

Addition of Acetic Acid to Camphenilene

A solution of 18 g (0.15 mole) of camphenilene in 70 ml of acetic acid containing 1 ml of 50% sulphuric acid was heated at 100° for 1 hour. The solution was poured into 500 ml of cold water and the two layers which formed were separated. The water layer was washed with ether and the ether washing combined with the organic layer. The resulting ether solution was washed with water, 10% sodium carbonate solution, and water and then dried over anhydrous magnesium sulphate. The ether solution was filtered and distilled to give 21 g of acetate product, b.p. $106-122^{\circ}$ at 30 mm. Chromatographic separation of the two major components which comprised 90% of the product was carried out, first with a Megachrom instrument fitted with six 8-ft apiezon J columns fitted in parallel to give two acetate products which were shown by chromatography to be 95% pure. Further purification of the acetates with an Aerograph unit fitted with a 10-ft dinonyl phthalate column gave the two components pure.

Acetate, b.p. 211° and n_D^{21} 1.4597. Calc. for $C_{11}\dot{H}_{18}O_2$: C, 72.53; H, 9.89. Found: C, 72.45; H, 9.66. Acetate, b.p. 214° and n_D^{21} 1.4611. Calc. for $C_{11}H_{18}O_2$: C, 72.53; H, 9.89. Found: C, 72.41; H, 9.77. The lower-boiling acetate was eluted first, on both columns.

The addition of acetic acid was carried out under a variety of conditions to determine the effect of time and temperature on the product ratio. For these experiments 1 g of camphenilene and 5 ml of acetic acid containing 1% of sulphuric acid were used. The results are given in Table II. A pure sample of the acetate,

Ľ	Ά	В	L	E	I	I

Time (min)	Temp. (°C)	% acetate of b.p. 211°	% acetate of b.p. 214°	Comment
20 60	60 60	$\frac{36}{39}$	$\begin{array}{c} 64\\61\end{array}$	Reaction incomplete 5% camphenilene
$5 \\ 30 \\ 240$	$100 \\ 100 \\ 100$	$35 \\ 39 \\ 43$	$\begin{array}{c} 65\\ 61\\ 57\end{array}$	Reaction complete

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b.p. 214°, was heated 5 minutes at 100° in acetic acid with sulphuric acid added. Work-up of the solution showed that there had been no isomerization of this acetate into the acetate, b.p. 211°. The product ratio is therefore kinetically controlled.

Hydroboration of Camphenilene

In a 200-ml 3-necked flask fitted with two gas adapters and a pressure-equalized dropping funnel was placed a solution of 10.73 g (0.088 mole) of camphenilene in 20 ml of purified diglyme. The flask was flushed with nitrogen, and 25 ml (0.025 mole) of 1 M sodium borohydride solution in diglyme was added. To the magnetically stirred solution was added dropwise a solution of 4.73 g (0.033 mole) of boron trifluoride etherate in 20 ml of diglyme over a 1-hour period. The solution was allowed to stand an additional hour and there was then added 7 ml of water and 14 ml of 3 N sodium hydroxide. The addition funnel was replaced by a condenser and 14 ml of 30% hydrogen peroxide was added in portions to maintain a steady reflux. The solution was cooled and added to 100 g of ice and extracted four times with water, and the ether extract was washed with ice water and dried over magnesium sulphate.

The ether solution was filtered and the ether removed by distillation. To the residual alcohol was added 40 ml of pyridine and 20 ml of acetic anhydride. The mixture was heated 3 hours on a steam bath and then poured into ice containing 15 ml of concentrated sulphuric acid. The resulting solution was extracted with ether and the ether solution washed with dilute sulphuric acid and water and then dried over magnesium sulphate. Distillation gave 9 g of acetate, b.p. $9\dot{5}$ –100° at 17 mm.

Vapor chromatographic separation of the product using a dinonyl phthalate column showed only 2 peaks. The first peak, $n_{\rm D}^{24}$ 1.4583, representing 45% of the total, was identical by infrared with the acetate. b.p. 211°, isolated from the addition reaction of acetic acid to camphenilene. The second peak, n_{D}^{24} 1.4600. representing 55% of the total, was identical with the acetate, b.p. 214°.

5-exo-Camphenilanol (β -Isofenchocamphorol)

A 15.1-g (0.0825 mole) sample of the acetate, b.p. 214°, which contained 5% of the acetate, b.p. 211°, was reduced in ether with 2.0 g of lithium aluminum hydride. After work-up in the usual way the dry ether solution of the alcohol product was reduced in volume to 20 ml, and 75 ml of pyridine was added. The resulting mixture was heated until all of the ethanol had distilled. Phthalic anhydride (11.3 g, 0.0825 mole) was added to the solution, which was then refluxed for 4 hours. The reaction mixture was poured into 1 liter of 10% sulphuric acid and extracted five times with 50-ml portions of benzene. The benzene solution was washed with water and dried. Evaporation of the benzene gave 23.3 g of product, m.p. 124-128°. Recrystallization from ethyl acetate and petroleum gave 10 g of the pure hydrogen phthalate of 5-exocamphenilanol, m.p. 130-131° (lit. (13) m.p. 130-131°).

A solution of 9.4 g of the hydrogen phthalate of 5-exo-camphenilanol and 12.5 g of sodium hydroxide in 50 ml of water was steam-distilled to give 3.9 g of 5-exo-camphenilanol, m.p. 53–54° (lit. (13) m.p. 60–61°). Sublimation raised the melting point to 55-56°.

Semicarbazone of 5-Camphenilanone

To a solution of 0.5 g of 5-exo-camphenilanol in 1.5 ml of acetone at 5° was added dropwise 1.3 ml of chromic acid solution containing 10.3 g of chromium trioxide and 8.7 ml of concentrated sulphuric acid in 30 ml of water. After 1 hour at 5° , addition was complete, and the reaction was diluted with 13 ml of water and extracted with ether. The ether extract was washed and dried and then concentrated to give 0.5 g of an oil. The oil was treated with 0.5 g of sodium acetate, 0.5 g of semicarbazide hydrochloride, 5 ml of water, and 5 ml of methanol and heated at 65° for 20 minutes. After addition of 10 ml of water and cooling, the semicarbazone separated. Recrystallization from methanol gave 0.25 g, m.p. 189-190°, of the semicarbazone of 5-camphenilanone.

6-exo-Camphenilanol

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A pure sample of 4 g of the acetate, b.p. 211°, was reduced with 1 g of lithium aluminum hydride in ether. After work-up in the usual way the product was distilled to give 2.8 g of 6-exo-camphenilanol, m.p. 30°, n_D³¹ 1.4187, and b.p. 200°. Cale. for C₉H₁₆O: C, 77.09; H, 11.50. Found: C, 77.13; H, 11.79.

The acid phthalate was prepared from a sample of the acctate, b.p. 211°, which contained 5% of the acetate, b.p. 214°, by the procedure used for the preparation of the hydrogen phthalate of 5-exo-camphenilanol. After three crystallizations from ethyl acetate and petroleum ether a constant melting point of 138.5-140° was obtained. Calc. for C17H20O4: C, 70.81; H, 6.99. Found: C, 71.02; H, 7.13.

6-Camphenilanone

A solution of 2.6 g of 6-exo-camphenilanol in 20 ml of ether was treated at 20° with 8.8 ml of a solution made up from 5.00 g of sodium dichromate dihydrate and 3.75 ml of concentrated sulphuric acid diluted to 25 ml by the procedure of Brown and Garg (21). Chromatography of the product showed two peaks. The major peak, representing 82% of the total, was collected to give 1.0 g of 6-camphenilanone, m.p. $55-56^{\circ}$ and b.p. 194° (lit. (18) b.p. 197°). Calc. for C₉H₁₄O: C, 78.21; H, 10.21. Found: C, 78.22; H, 9.95.

Semicarbazone, m.p. 183-184°, mixed m.p. with the semicarbazone of 5-camphenilanone 159-172°. Calc. for C10H17N3O: C, 61.51; H, 8.78; N, 21.52. Found: C, 61.46; H, 8.66; N, 21.50. The semicarbazone, which

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was prepared in methanol-water with semicarbazide hydrochloride and sodium acetate at room temperature, precipitated over a period of 4 weeks.

2,4-Dinitrophenylhydrazone, m.p. 164–165°. Calc. for $C_{15}H_{18}N_4O_4$: C, 56.59; H, 5.70; N, 17.60. Found: C, 56.65; H, 5.53; N, 17.61. The 2,4-dinitrophenylhydrazone took 3 weeks to form by the procedure of Shine (22). Camphor under the same conditions yields the derivative in 3 days.

The minor peak was collected but not identified. Analysis gave C, 72.09; H, 8.08.

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