Additions to Bicyclic Olefins. III. Stereochemistry of the Epoxidation of Norbornene, 7,7-Dimethylnorbornene, and Related Bicyclic Olefins. Steric Effects in the 7,7-Dimethylnorbornyl System

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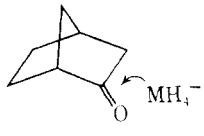
Abstract: A systematic study of the stereochemistry of epoxidation of norbornene, 7,7-dimethylnorbornene, and related bicyclic olefins was undertaken in order to establish more precisely the importance of steric effects in controlling the direction of concerted additions to such systems. The epoxidation of norbornene proceeds almost exclusively exo, 99%, whereas the corresponding epoxidation of 7,7-dimethylnorbornene takes place preferentially from the opposite direction, 88–94% endo. 1-Methylnorbornene, 2-methylnorbornene, and 1,7,7-trimethylnorbornene exhibit the same steric pattern of reaction. Similarly, epoxidation of the exocyclic double bond in 2-methylenenorbornane gives the *exo*-epoxide preferentially, 86%, whereas the related 2-methylene-7,7-dimethylnorbornane gives the endo isomer preferentially, 84%. Therefore, in the case of concerted additions, such as the epoxidation reaction of the present study and the hydroboration reaction of an earlier study, the normal course of addition to olefins of the norbornene type is almost exclusively exo in the absence of 7,7-dimethyl substituents, and predominantly endo in their presence. This controlling influence of the 7,7-dimethyl substituents is exerted even in the case of these concerted additions to the exocyclic double bonds of 2-methylenenorbornane and 2-methylene-7,7-dimethylnorbornane.

It has been argued that the almost exclusive exo substitution realized in the solvolysis of 7,7-dimethylnorbornyl derivatives requires the intermediacy of a σ-bridged norbornyl cation.[3,4] This position was based on the observation that complex metal hydrides, such as lithium aluminum hydride[5] and sodium borohydride,[6] attack norcamphor preferentially from the exo direction (**1**), whereas these reagents attack 7,7-dimethylnorcamphor preferentially from the endo direction (**2**). In contrast, solvolyses of both norbornyl



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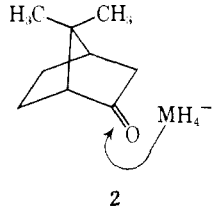

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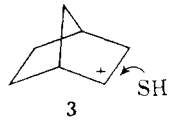
(**3**) and 7,7-dimethylnorbornyl (**4**) derivatives, proceeding through the corresponding ions or ion pairs, give the exo products almost exclusively. It was proposed



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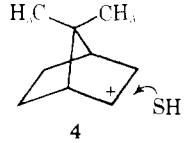

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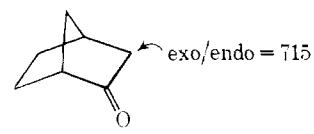
that the failure of the 7,7-dimethyl substituents to control the stereochemistry of substitution in the cation (or ion pair) in the same manner that these methyl groups control the direction of attack by complex hydride required something "special,"[3,4] σ bridging in the cation (or ion pair).

However, it was pointed out that very little is known about the relative steric requirements for the reaction of complex hydrides with ketones and the reaction of cations or ion pairs with solvents.[7] In fact, recent studies demonstrate that in the base-catalyzed deuterium exchange exo substitution is favored in both norcamphor (**5**) and camphor (**6**),[8,9] a reaction which cannot involve σ-bridged intermediates.



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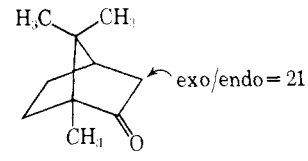

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It appeared desirable to undertake a systematic study of reactions of norbornene and 7,7-dimethylnorbornene derivatives in order to realize a better understanding of the precise factors influencing the direction of reaction in the norbornyl system, and the precise influence of 7,7-dimethyl substituents on the stereochemical course. Accordingly, we have examined hydroboration,[10] epoxidation (reported in the present paper), oxymercuration,[11] hydrochlorination,[12] and other addition reactions of norbornene, 7,7-dimethylnorbornene, and

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(2) Postdoctorate research associate on a grant (GP 6492 X) supported by the National Science Foundation.

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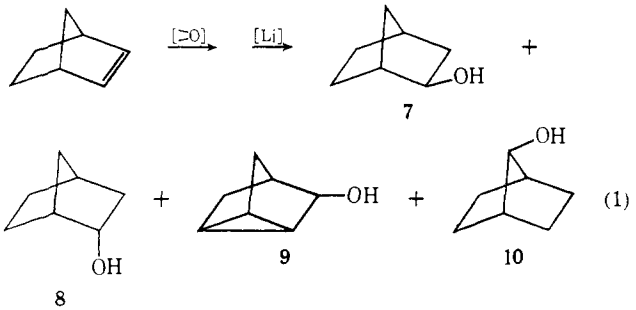
related olefins.[13] These studies have led us to a new, promising interpretation of the steric influence of the 7,7-dimethyl substituents in reactions of the norbornyl system[14] and has provided a considerable amount of new information which will have to be accounted for in a complete theory of the behavior of the norbornyl cation. This paper presents the results of our study of the stereochemistry of epoxidation of norbornene, 7,7-dimethylnorbornene, and related olefins.

Results and Discussions

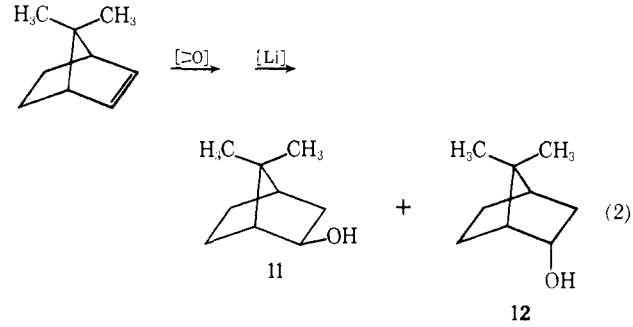
The epoxidation of norbornene has been previously described in the literature,[15] but no unequivocal data for the precise amount of exo and endo isomers in the epoxide product has been reported. In part, this deficiency arises from the tendency of these labile epoxides to rearrange or decompose while being analyzed by gas chromatography.[16] It might be considered that this difficulty could be overcome by reduction of the epoxides to the isomeric alcohols, followed by glpc analysis of the latter. However, the usual lithium aluminum hydride reduction of norbornene oxide to form the alcohol is very slow and is often accompanied by rearrangement.[17]

Fortunately, we were able to circumvent these difficulties. First, we established glpc conditions which permitted us to analyze norbornene oxide and many related bicyclic epoxides, without the complicating rearrangements or decompositions that had troubled earlier workers.[16] Second, we developed a new convenient procedure for the facile reduction of such epoxides without rearrangement, utilizing lithium in ethylenediamine.[18] These developments permitted us to determine precisely the stereochemistry of epoxidation of norbornene, 7,7-dimethylnorbornene, and related bicyclic olefins.

The epoxidation of norbornene with *m*-chloroperbenzoic acid in methylene chloride at 25° for 1 hr, followed by reduction of the product with lithium in ethylene diamine (eq 1), gives an 87% yield of 99.0% *exo*-norbornanol (**7**), 0.3% *endo*-norbornanol (**8**), 0.5% nortricyclanol (**9**), and 0.2% 7-norbornanol (**10**), indicating almost exclusive exo addition. In contrast,



the epoxidation of 7,7-dimethylnorbornene at 25° for 27 hr, followed by reduction (eq 2), gives an 87% yield of 6% *exo*- (**11**) and 94% *endo*-7,7-dimethylnorbornanol (**12**), indicating a strong preference for endo addition.



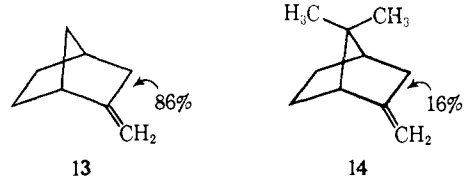
Analysis of the norbornene epoxide by both glpc and pmr indicated the presence of the exo isomer in a yield in the range of 98–99.5%. Consequently, the three methods indicate almost exclusive exo attack by the reagent (~99%). Similarly, both glpc and pmr examination of the product from epoxidation of 7,7-dimethylnorbornene indicated the presence of 12% of the exo isomer. This is higher than the 6% indicated by the lithium ethylenediamine method. However, the results clearly indicate that the epoxidation of this olefin occurs preferentially endo (88–94% endo).

Competitive epoxidation experiments indicated that norbornene reacts with *m*-chloroperbenzoic acid at a rate approximately 100 times that of 7,7-dimethylnorbornene.

If we assign k_{endo} for norbornene, an arbitrary value of 1.00, then k_{exo} in norbornene will have a value of 100–200, k_{exo} in 7,7-dimethylnorbornene will have a value of roughly 0.1, and k_{endo} in 7,7-dimethylnorbornene will also have a value of approximately one, very similar to that for k_{endo} norbornene. Consequently, the presence of the 7,7-dimethyl substituents decreases the rate of exo attack of the reagent by a factor of approximately 1000, causing the reaction to proceed predominately endo, and causing the overall rate to be slower by a factor of approximately 100.

Similar stereochemical results were realized with 1-methylnorbornene (99% exo), 2-methylnorbornene (99.5% exo), and 1,7,7-trimethylnorbornene (5% exo). Consequently, we appear to be observing a consistent pattern of behavior.

The stereochemical influence of the 7,7-dimethyl substituents is exerted in this reaction even when the double bond is exocyclic, at the corner of the bicyclo[2.2.1]heptane structure. Thus, 2-methylenenorbornane (**13**) gives 86% *exo*-epoxide, whereas 2-methylene-7,7-dimethylnorbornane (**14**) gives 84% endo product.



The experimental results are summarized in Table I.

These data reveal a remarkable stereochemical preference of at least 100:1 for the exo epoxidation of norbornene in a reaction which does not involve a car-

(13) For detailed reviews of electrophilic additions to olefins, with pertinent literature references, see R. C. Fahey, *Top. Stereochem.*, **3**, 237 (1968); P. B. D. de la Mare and R. Bolton, "Electrophilic Additions to Unsaturated Systems," Elsevier, Amsterdam, 1966; T. G. Traylor, *Accounts Chem. Res.*, **2**, 152 (1969).

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Table I. Epoxidation of Substituted Norbornenes

Olefin	*Anal.* of epoxide, % exo		*Anal.* of alcohol, %[a]	
	Glpc	Pmr	Yield	Exo
Norbornene (**1**)	(98)[b]	99.5	87	99
7,7-Dimethylnorbornene (**2**)	12	12	87	6
1-Methylnorbornene	99		88	99[c]
2-Methylnorbornene	100		100	99.5[c]
1,7,7-Trimethylnorbornene	4.4		80	5[c]
2-Methylenenorbornane (**13**)	87		86	86
2-Methylene-7,7-dimethylnorbornane (**14**)			89	16

[a] By glpc, after reduction of epoxide by lithium in ethylenediamine. [b] See Experimental Section. [c] These epoxides yield a mixture of position isomers on reduction.

bonium ion intermediate.[19] We had previously suggested that simple steric considerations can be used to account for the greater reactivity of U-shaped molecules which have a relatively open exo face and a hindered endo face.[20] It has also been suggested that torsional effects may also contribute to the observed stereochemistry.[21]

In any event, the available results now reveal that both hydroboration and epoxidation of norbornene exhibit a major preference for attack at the exo face of the bicyclic structure, a preference that is in the range of 100:1–200:1. An even larger preference for exo over endo, 715:1, is reported by Tidwell for the base-catalyzed deuteration of norcamphor.[9] It follows that the norbornane structure can exhibit major preferences for reaction from the exo direction in representative noncarbonium ion reactions. Since these reactions cannot possibly involve σ bridging, it is quite clear that some other property of the rigid bicyclic norbornane structure gives reaction at the exo face a marked preference over reaction at the endo face, a preference that may vary considerably with the nature of the reaction.

But what about the 7,7-dimethylnorbornyl system? The present results on hydroboration and epoxidation reveal quite clearly that the 7,7-dimethyl substituents exert a dominant influence on the stereochemistry of such concerted additions. Moreover, although phenyl azide reacts readily with norbornene in a similar cis addition, 7,7-dimethylnorbornene fails to react after 14 days at 100°.[22,23] These results clearly indicate that for such concerted addition reactions attack of the double bond from both the endo and the exo direction are strongly hindered in 7,7-dimethylnorbornene. Such reactions in this system either occur preferentially from the endo direction, or they fail to take place at all.

The directive influence of both the norbornane structure and of the 7,7-dimethyl substituents is considerably less for the exocyclic double bond than for the endocyclic double bond for these concerted additions. Thus, 2-methylenenorbornane (**13**) achieves only 86% *exo*-epoxide and 7,7-dimethyl substituents (**14**) change this modest exo preference to a modest endo preference, 84% *endo*-epoxide. If we assume that k_{endo} for **13** and **14** are essentially identical, as they evidently are for norbornene and 7,7-dimethylnorbornene, then the value of k_{exo} decreases by a factor of 36 for the introduction of the 7,7-dimethyl substituents. This compares with a decrease by a factor of 1000 previously estimated for the endocyclic derivatives.

Conclusions

The present results support the position that for such concerted addition reactions the 7,7-dimethyl substituents dominate the stereochemistry of the addition. Consequently, the results lend apparent support to the original position that the failure of 7,7-dimethyl substituents to invert the stereochemistry of addition to the cation (**3**, **4**) must require some "special" feature, namely, σ bridging.[3,4]

However, such concerted additions are evidently reactions of large steric requirements. Consequently, we should consider the possibility that by utilizing a concerted addition of sufficiently low steric requirements, we might be able to achieve preferential exo reaction in both 2-methylenenorbornane (**13**) and 2-methylene-7,7-dimethylnorbornane (**14**). Indeed, the analogy would be even closer to the reaction of solvent with the cation or ion pair (**3**, **4**) were we to explore the stereochemistry of nonconcerted "two-stage" additions to these norbornene olefins. Even though the reaction is of a different type, the observation of preferential exo deuteration of camphor,[5,9] in spite of the steric influence of the 7,7-dimethyl substituents, is highly significant. Consequently, we are extending our studies of additions to include such nonconcerted, two-stage processes.

Experimental Section

Materials. Anhydrous ethylenediamine from Fisher Scientific was used without further treatment. The *m*-chloroperbenzoic acid was from F. M. C. Corporation.

Spectra. The nuclear magnetic resonance spectra were obtained on the Varian A60A.

Gas Chromatography (glpc). The analyses were carried out on the Perkin-Elmer 226 fitted with a 150 ft × 0.01 in. Golay column. Authentic samples[10] were used to identify alcohols obtained from the reduction of the corresponding epoxides.

General Procedure for the Epoxidation of Olefins. To a 100-ml three-necked flask fitted with a septum outlet, thermometer, and magnetic stirring bar was added 20 ml of methylene chloride and 2.15 g (10 mmol) of 80% *m*-chloroperbenzoic acid.[24] To this stirred slurry was added 10 ml of olefin dissolved in 10 ml of methylene chloride at such a rate to keep the temperature about 25° in 5–10 min. When the reaction mixture gave a negative starch–iodine test, 20 ml of 10% aqueous sodium carbonate was added and the mixture was stirred vigorously for *ca.* 30 min at room temperature. Separation of the organic layer, drying over magnesium sulfate, and evaporating the solvent at room temperature on a rotatory evaporator, gave the epoxide.

General Procedure for Reduction of Epoxides. The crude epoxides were quantitatively reduced without rearrangement to their corresponding alcohols by a convenient lithium–ethylenediamine reduction.[18] The alcohols were extracted with tetrahydrofuran and an internal standard was added to determine the yield by glpc.

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(20) H. C. Brown, W. J. Hammer, J. H. Kawakami, I. Rothberg, and D. L. Vander Jagt, *J. Amer. Chem. Soc.*, **89**, 6381 (1967).

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(22) (a) K. Alder and G. Stein, *Justus Liebigs Ann. Chem.*, 185, 515 (1935); (b) P. Scheiner, J. H. Schomaker, S. Deming, W. J. Libby, and G. P. Nowak, *J. Amer. Chem. Soc.*, 87, 306 (1965).

(23) Similarly, chlorosulfonyl isocyanate adds readily to norbornene, but fails to add to bornylene: E. J. Moriconi and W. C. Crawford, *J. Org. Chem.*, 33, 370 (1968).

(24) The sample contained 20% *m*-chlorobenzoic acid.

Epoxidation–Reduction of Norbornene. The epoxidation of 0.94 g (10 mmol) of norbornene with 2.20 g (10 mmol) of 78% *m*-chloroperbenzoic acid was complete within 20 min, but stirred at room temperature for 1 hr. Reduction with lithium–ethylenediamine and analysis on UCON LB 550X at 100° indicated 99.0% *exo*-norbornanol, 0.3% *endo*-norbornanol, 0.5% nortricyclanol, and 0.2% 7-norbornanol in 87% yield in order of increasing retention time. Presumably, the latter two alcohols result from side reactions on *exo*-norbornene oxide.[16,19]

Analysis of the epoxide before reduction on UCON LB 550X at 100° with an injection-block temperature of 170° indicated a major peak of 98% and a minor peak of 2%. At a block temperature of 200°, the minor peak increased to *ca.* 4%. The irregular and broad minor peak had a retention time different from that of norcamphor.

Analysis by nmr of 200 mg of crude epoxide in a minimum of carbon tetrachloride indicated 99.5% *exo*-norbornene oxide at 2.87 ppm and 0.5% *endo*-norbornene oxide at 3.4 ppm. The singlet peaks were measured using the bridgehead proton as an internal standard. No change in the minor peak tentatively assigned to the α-methine protons of *endo*-epoxide was observed by the addition of deuterium oxide. The infrared in carbon disulfide indicated a strong doublet band at 11.84 μ.[25] Sublimation of the epoxide gave mp 123–125° (lit.[15c] mp 125.5–126.5°).

Anal. Calcd for $C_7H_{10}O$: C, 76.32; H, 9.15. Found: C, 76.17; H, 9.41.

Epoxidation–Reduction of 2-Methylenenorbornane (13). Epoxidation of 2-methylenenorbornane in 1 hr and reduction with lithium gave an 86% yield of 86% 2-*exo*- and 14% 2-*endo*-2-methyl norbornanol on Quadrol at 100°. The analysis of the crude epoxide at 80° on UCON LB 550X indicated 87% major and 13% minor addition products.

Epoxidation–Reduction of 7,7-Dimethylnorbornene. Epoxidation of 0.608 g (5 mmol) of 7,7-dimethylnorbornene with 1.105 g (5 mmol) of 78% *m*-chloroperbenzoic acid for 27 hr at room temperature, followed by reduction with lithium, gave an 87% yield of alcohol, 2% 5,5-dimethyl-, 2% 6,6-dimethyl-2-*exo*-norbornanol, *ca.* 6% 2-*exo*-7,7-dimethylnorbornanol (**11**), and 90% 2-*endo*-7,7-dimethylnorbornanol (**12**). This gives 94% endo and 6% exo addition. Another run gave a 100% yield of 5% exo (**11**) and 95% endo (**12**). The analysis was on UCON LB 550X at 60–120° at 10°/min with **11** coming out just before **12**.

Analysis of the crude epoxide on UCON LB 550X at 100° with the injection block at 150° indicated *ca.* 88% major and 12% minor product, in order of increasing retention time: nmr (CCl_4) δ 0.84 and 1.20 (sharp methyl singlets), 2.98 (8%), and 3.42 (92%) [broad singlet (α-methine proton of isomeric epoxides)]; ir (CS_2) 11.57 μ (strong).[25] Sublimation gave the epoxide, mp 100–107°.

Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.13; H, 10.29.

Epoxidation–Reduction of 2-Methylene-7,7-dimethylnorbornane (14). The epoxidation of **14** at room temperature in 1 hr, neutralization of the acid at 0° with sodium carbonate, and reduction with lithium–ethylenediamine gave 16% of 2,7,7-trimethyl-2-*exo*-norbornanol and 84% of 2,7,7-trimethyl-2-*endo*-norbornanol in 88.5% yield. The glpc analyses were on UCON LB 550X at 120° and Carbowax 20M at 100°. Authentic alcohols were prepared by the reaction of the methyl Grignard on 7,7-dimethylnorcamphor. The epoxides decomposed under our glpc conditions.

Epoxidation–Reduction of 1-Methylnorbornene. Epoxidation–reduction yielded 88% alcohols: 60% 2-*exo*-, 39% 3-*exo*-, and 0.8% 2-*endo*- and 3-*endo*-1-methylnorbornanol. Glpc analyses were on UCON LB 550X at 130°.

Epoxidation–Reduction of 1,7,7-Trimethylnorbornene. The epoxidation–reduction of the olefin in 25 hr gave an 80% yield of alcohols: 3.5% isobornanol, 47.6% bornanol, 1.3% epiisobornanol, and 47.6% epibornanol, in increasing order of retention time on UCON LB 550X at 130°. Glpc analysis of the crude epoxide at 110° indicated 95.6% *endo*- and 4.4% *exo*-oxide; nmr (CCl_4) δ 3.4 [quartet (α-methine *endo*-epoxide)], 3.1 [doublet, J = 4 cps (α-methine *exo*-epoxide)], and 0.77, 0.965, and 1.08 (major methyl singlets).

Epoxidation–Reduction of 2-Methylnorbornene. Epoxidation–reduction gave a 100% yield of 71.1% 2-*exo*-, 0.5% 2-*endo*-2-methylnorbornanol, and 28.4% 3-*endo*-methyl-2-*exo*-norbornanol. Glpc was on Quadrol at 100°.

Isolation of Norbornene Oxide under Nonaqueous Conditions. After the epoxidation of norbornene in the usual manner, the reaction mixture was cooled to −20°, and *m*-chlorobenzoic acid was filtered. The solvent was evaporated at room temperature and a small amount of pentane was added to dissolve the epoxide, and the remaining white solid filtered off. The pentane was evaporated and the nmr (CCl_4) indicated greater than 99% *exo*-norbornene oxide.

Competitive Epoxidation between Norbornene and 7,7-Dimethylnorbornene. To a 20-ml flask equipped with a magnetic stirring bar was added 8.0 ml of a solution in methylene chloride of 0.825 mmol of norbornene and 0.845 mmol of 7,7-dimethylnorbornene. To this stirred solution was added 0.9 ml (0.2 mmol) of *m*-chloroperbenzoic acid in methylene chloride. In 90 min, 5 ml of 10% aqueous sodium carbonate was added and the epoxide solution separated and dried. The calibrated epoxide ratio was 113:1 or 99.12% norbornene oxide and 0.88% 7,7-dimethylnorbornene oxide.

(25) W. A. Patterson, *Anal. Chem.*, **26**, 823 (1954).