on 25 g of silica gel using chlofoform containing 2% methanol as the eluent for inspection by thin layer chromatography.

Evaporation of appropriate fractions gave 870 mg of yellow-orange crystals which were recrystallized from chloroform–benzene to give 671 mg of **6** as colorless needles: mp 176–178° dec; ν_{max} 3500 (OH), 1656 (C=O), 1618 cm^{-1} (C=C); λ_{max} 232 (log ϵ 4.04), 278 mμ (log ϵ 4.03); nmr τ 7.65 (N–CH_3, 3 H, s), 6.44 and 6.37 (olefinic O–CH_3, 3 H, s), 4.16 and 4.0 (olefinic protons, 2 H, a pair of d), 3.57 (aromatic proton, 1 H, s). The mass spectrum showed the molecular ion at m/e 371.

Anal. Calcd for $C_{21}H_{25}NO_5 \cdot {}^1/_2C_6H_6$:[19] C, 70.21; H, 6.87. Found: C, 69.90; H, 7.26.

(19) The presence of benzene was confirmed by the peak at τ 2.68 ($^1/_2$ C_6H_6, 3 H, s) in the nmr spectrum and the ion at m/e 78 in the mass spectrum.

Registry No.—**3** hydrochloride, 14897-72-4; **4** hydrochloride, 14897-73-5; **6**, 14897-76-8; **7b**, 14897-77-9; **8a**, 1135-23-5; **8b**, 14897-78-0; **9a**, 14897-79-1; **9b**, 14897-80-4; **10a**, 15038-85-4; **10b**, 15038-86-5; **11a**, 14897-81-5; **11b**, 14897-82-6; **12a**, 14924-44-8; **12b**, 15038-87-6; **13a** hydrochloride, 14924-45-9; **13b** hydrochloride, 14924-46-0.

Acknowledgment.—We wish to express our gratitude to Miss R. Hasebe and Miss T. Yamaki for the microanalyses, and Miss Y. Tadano for the nmr determinations.

The Preparation and Study of Some 1-Norbornenyl and Norbornenyl-1-carbinyl Derivatives[1,2]

JAMES W. WILT, CHARLES T. PARSONS, CHARLES A. SCHNEIDER, DAVID G. SCHULTENOVER, S. J., AND WILLIAM J. WAGNER

Department of Chemistry, Loyola University, Chicago, Illinois 60626

Received May 16, 1967

As part of a general program to investigate the inductive effect of the vinyl group apart from its resonance effect, the synthesis and properties of a fair number of 1-norbornenyl and norbornenyl-1-carbinyl derivatives are described. It is felt that these compounds, by their structure, have the resonance effect of the double bond effectively cancelled and by their reactivity exhibit the true inductive effect of the linkage. The syntheses of these substances proceeded principally from norbornene-1-carboxylic acid (**5**). The preparation of **5** is described in detail from *exo*-2-bromonorbornane-1-carboxylic acid (**6**). As the process can lead to norbornene-2-carboxylic acid (**7**) instead, conditions leading to either acid are delineated. Among the other compounds prepared and characterized were the amine salt (**12**), the acetate (**23**), the chloride (**27**), the phenyl ketone (**34**), the aldehyde (**35**), the carbinol (**37**), and the acetic acid (**40**). Several mechanistic studies were performed. First, the bridgehead chloride **27** exhibited no displacement reactivity even though it is formally an allylic chloride. Second, the hydrolysis of norbornenyl-1-carbinyl tosylate (**38**) in aqueous acetone was about 16 times slower at 25° than the saturated analog **42**, a direct experimental confirmation of the heretofore calculated inductive effect of the homoallylic double bond. When *sym*-collidine was present in the solvent, the composition of the hydrolysate was unrearranged **37** (42%), and a new alcohol, bicyclo[3.2.1]oct-6-en-1-ol (**44**, 58%), was isolable in high yield. Only the latter alcohol was obtained in the absence of collidine because **37** underwent decomposition. Lastly, generation and decomposition of the norbornenyl-1-carbinyl diazonium ion from the tosylhydrazone **36** *via* an alkaline treatment of it in N-methylpyrrolidone again gave a product composed of **44** (47%), but, in addition, bicyclo[2.2.2]oct-2-en-1-ol (**43**, 44%) was also formed. This reaction is yet another example of alcohol formation in tosylhydrazone decompositions. The relative tendencies of the methano and ethano bridges to migrate in these reactions is discussed, with emphasis on the strain relieved and the delocalization possible in the transitional species. No evidence for etheno bridge migration was found in either reaction.

Considerable activity has centered in norbornene chemistry for some time.[3] The fixed geometry[4] of the ring has allowed the study of mechanistic items of interest such as π participation in the solvolysis of the *anti*-**7** and *exo*-**5** brosylates[5] and chlorides,[6] as well as in several norbornenylcarbinyl substrates.[7] Oddly enough, with all the work done in the area, only a few examples of 1-norbornenyl or norbornenyl-1-carbinyl derivatives exist in the literature. Most significantly, Bly and co-workers[8] have independently also investigated the norbornenyl-1-carbinyl system in solvolysis and deamination reactions. In addition, 1-methylnorbornene (**1**) is known,[9a] but only recently has some of its chemistry been reported.[9b] And lastly, 1-norbornenol (**2**) was prepared some years ago[10] and

(1) Taken from the dissertations of C. A. S. (June 1964) and W. J. W. (June 1967).

(2) (a) *Cf.* J. W. Wilt and C. A. Schneider, *Chem. Ind.* (London), 951 (1963), for a preliminary account of some of this material. (b) Presented in part at the 148th National Meeting of the American Chemical Society, Chicago, Ill., Sept 1964, Abstracts, Paper 79S.

(3) Much carbonium ion chemistry of norbornene may be found in J. A. Berson, "Molecular Rearrangements," Part I, P. deMayo, Ed., Interscience Publishers, New York, N. Y., 1963, p 111 ff.

(4) The geometry is apparently not known definitely. The data applied to norbornene have been determined on other, more or less related compounds. *Cf.* K. Tori, R. Muneyuki, and H. Tanida, *Can. J. Chem.*, **41**, 3142 (1963).

(5) S. Winstein, H. M. Walborsky, and K. C. Schreiber, *J. Am. Chem. Soc.*, **72**, 5795 (1950); S. Winstein, M. Shatavsky, C. J. Norton, and R. B. Woodward, *ibid.*, **77**, 4183 (1955); see also, H. Tanida, T. Tsuji, and T. Irie, *J. Org. Chem.*, **31**, 3941 (1966).

(6) J. D. Roberts and W. Bennett, *J. Am. Chem. Soc.*, **76**, 4623 (1954); W. G. Woods, R. A. Carboni, and J. D. Roberts, *ibid.*, **78**, 5653 (1956).

(7) For the *syn*- and *anti*-7-carbinyl brosylates, see R. K. Bly and R. S. Bly, *J. Org. Chem.*, **31**, 1577 (1966); for the *exo*- and *endo*-2-carbinyl brosylates and carbinylamines, see R. R. Sauers, R. A. Parent, and H. M. How, *Tetrahedron*, 2907 (1965).

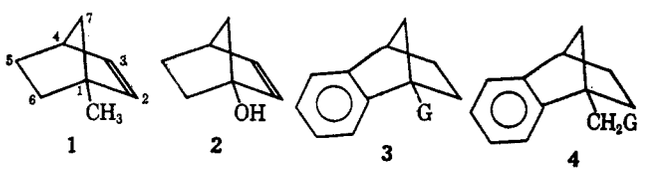
(8) (a) R. S. Bly and Q. E. Cooke, 148th National Meeting of the American Chemical Society, Chicago, Ill., Sept 1964, Abstracts, Paper 80S; (b) R. S. Bly and E. K. Quinn, 153rd National Meeting of the American Chemical Society, Miami Beach, Fla., April 1967, Abstracts, Paper 91O. We appreciate the details of these comprehensive studies from Professor Bly and the several discussions with him throughout the course of this study.

(9) (a) M. Blanchard, *Bull. Soc. Chim. France*, 1264 (1961). It should be mentioned that the isomeric 2-methylnorbornene is misnamed the 1 isomer in various parts of a recent paper by W. F. Erman, *J. Org. Chem.*, **32**, 765 (1967). (b) Oxymercuration–demercuration: H. C. Brown, J. H. Kawakami, and S. Ikegami, *J. Am. Chem. Soc.*, **89**, 1525 (1967). Hydrochlorination; H. C. Brown and K.-T. Liu, *ibid.*, **89**, 3898 (1967). Protonic acid additions: P. von R. Schleyer, *ibid.*, **89**, 3901 (1967).

(10) C. J. Norton, Dissertation, Harvard University, 1955.

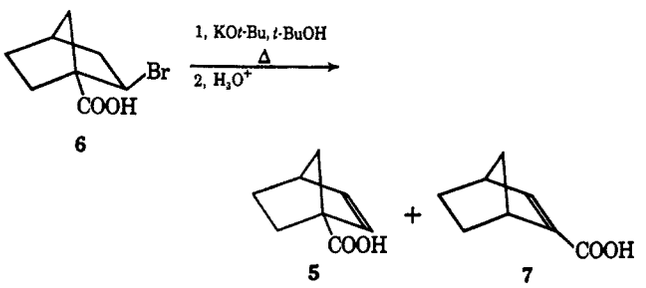
shown to be devoid of solvolytic reactivity. Other than for these, and for some highly substituted (usually chlorinated) examples available through Diels–Alder reactions of various cyclopentadiene derivatives with suitable dienophiles,[11] no information appears available on the methods of synthesis and reactivity of such materials.

Our interest in this matter arose in connection with attempts to modify the rearrangement ability of the phenyl ring in certain radical and cationic rearrangements by restricting its rotation, using various alicyclic rings[12] and finally a bicyclic ring[13] to achieve this. The synthetic problems involved in the latter, specifically the attempted construction of 1-benzonorbornenyl (**3**) and benzonorbornenyl-1-carbinyl (**4**) types of compounds, led us to construct first the corresponding norbornene derivatives.



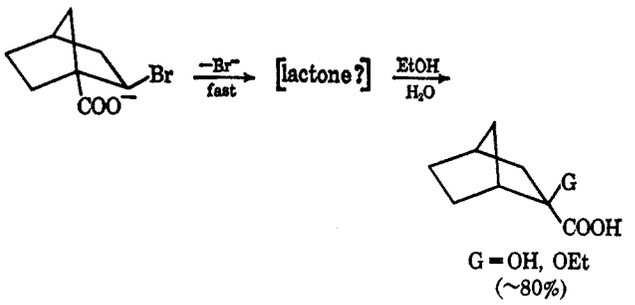
1 2 3 4

I. Chemistry of 1-Norbornenyl Derivatives. Norbornene-1-carboxylic Acid (5).—In view of the great synthetic utility of the carboxyl function, a desirable starting compound in this work would be the heretofore unknown norbornene-1-carboxylic acid (**5**). A straightforward preparation of this acid would involve dehydrobromination of *exo*-2-bromonorbornane-1-carboxylic acid (**6**), a known compound prepared first in 1958 as the product of an interesting Wagner–Meerwein rearrangement in the Hell–Volhard–Zelinsky bromination of either *exo*- or *endo*-norbornane-2-carboxylic acid.[14] It was found, however, that reaction of **6** with potassium *t*-butoxide in hot *t*-butyl alcohol led to mixtures of **5** and the conjugated isomer, norbornene-2-carboxylic acid (**7**), the latter being the sole product under certain conditions. In the course of other concurrent work on



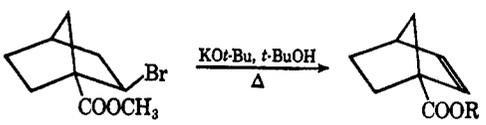
6 5 7

the solvolytic reactivity of 1-substituted *exo*-2-norbornyl derivatives,[15] it was found that bromide ion loss from the anion of **6** was faster than from *exo*-2-norbornyl bromide in 80% ethanol. The products were largely rearranged (80% were norbornane-*endo*-2-carboxylic acid derivatives), indicating that the carboxylate function participated in bromide loss, possibly *via* an α- or β-lactone. To decrease this



G = OH, OEt
(~80%)

participation and thereby the consequent rearrangement, **6** was converted into its methyl ester **8**,[16] most simply by using methyl sulfate instead of the diazomethane used before.[14] As hoped, dehydrobromination of **8** under the same conditions as employed for **6** indeed did lead to the desired unsaturated ester **9**, although considerable transesterification to the *t*-butyl ester **10** also occurred. The mixture of esters was



8

9, R = CH_3
10, R = *t*-Bu

readily saponified, nonetheless, and the desired bridgehead acid **5** was obtainable in 90% yield from **8**. The structure of this acid was uniquely evident from its spectra. The infrared absorption of the acid carbonyl was at 5.85 μ (unconjugated) and the nmr spectrum showed two vinyl protons centered at δ 6.2 and one bridgehead proton centered at δ 3.0. Acid **5** is a colorless, malodorous crystalline compound, mp 95–96°. Its phenacyl ester was easily prepared, mp 69–70.5°. Its acidity (pK_A = 5.98 in 50% ethanol[17]) is about 2.5 times greater than that of norbornane-1-carboxylic acid (**11**, pK_A = 6.31[17]), a compound known for some time.[18] Hydrogenation of **5** readily afforded **11**. On the other hand, the conjugated acid **7**, isolated in good yield from the dehydrobromination of **6**, possessed the typical conjugated acid carbonyl at 5.94 μ and only one vinyl proton centered at δ 7.1, together with two bridgehead protons centered at δ 3.05 and 3.25 in the nmr spectrum.[19] Differentiation

(11) *Inter alia*, chlordene, aldrin, and heptachlor. For some simpler examples, see C. F. Wilcox, Jr., and J. G. Zajacek, *J. Org. Chem.*, **29**, 2209 (1964).

(12) See J. W. Wilt, L. L. Maravetz, and J. F. Zawadzki, *ibid.*, **31**, 3018 (1966), and references therein for studies on 1-phenylcycloalkylcarbinyl systems, and J. W. Wilt and C. A. Schneider, *ibid.*, **26**, 4196 (1961), for a study of the 1-methylindanylcarbinyl system.

(13) J. W. Wilt, C. A. Schneider, J. P. Berliner, and H. F. Dabek, Jr., *Tetrahedron Letters*, 4073 (1966).

(14) (a) W. R. Boehme, *J. Am. Chem. Soc.*, **80**, 4740 (1958); **81**, 2762 (1959); (b) H. Kwart and G. Null, *ibid.*, **80**, 248 (1958); **81**, 2765 (1959). For the application of this rearrangement to prepare 2-axial-bromobicyclo-[3.2.1]octane-1-carboxylic acid, see A. W. Chow, D. R. Jakas, and J. R. E. Hoover, *Tetrahedron Letters*, 5427 (1966).

(15) J. W. Wilt and W. J. Wagner, in preparation. In this paper the mechanism of the dehydrobromination of **6** will be detailed.

(16) Neighboring group participation is normally reduced in importance when the carboxylate function is converted into an ester. For example, whereas the solvolysis of α-bromopropionate ion is a classic example of carboxylate ion participation, the solvolysis of ethyl α-bromopropionate proceeds with negligible participation by the carboethoxy function: E. S. Gould, "Mechanism and Structure in Organic Chemistry," H. Holt and Co., Inc., New York, N. Y., 1959, p 563 ff. Ester participation is nonetheless often observed, particularly in the alkyl portion of the ester, as in the acetolysis of *trans*-2-acetoxycyclohexyl tosylate. Such participation in the acyl portion of an ester is less common, but it has been observed, *e.g.*, in the increased rate of solvolysis of phenyl *o*-(α-bromobenzyl)benzoate compared to its *para* isomer: B. Capon, *Quart. Rev.* (London), **18**, No. 1, 68 (1964).

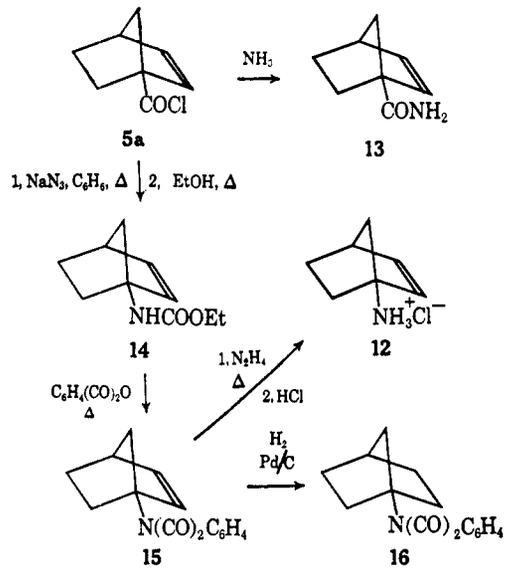
(17) We thank Mr. H. Dabek, Jr., for these determinations.

(18) (a) W. P. Whelan, Jr., Dissertation, Columbia University, 1952; (b) R. L. Bixler and C. Niemann, *J. Org. Chem.*, **23**, 742 (1958).

(19) During the course of this work, the conjugated acid was described by R. A. Finnegan and R. S. McNees, *Chem. Ind.* (London), 1450 (1961); *J. Org. Chem.*, **29**, 3234 (1964). We thank Professor Finnegan for certain spectra and a sample of the amide of **7** which were used to confirm the nature of our material.

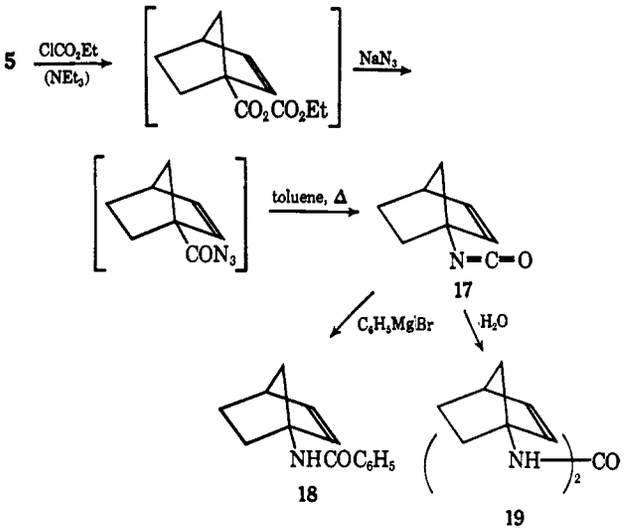
of these acids and further confirmation of their structures were possible *via* their methyl esters (see Experimental Section).

1-Norbornenylamine.—Subsequent reactions on **5** were aimed at the synthesis of 1-norbornenyl and norbornenyl-1-carbinyl derivatives that would serve as reference compounds for their benzonorbornenyl analogs.[18] One such substance was 1-norbornenylamine, as its salt **12**. Preparation of this salt was effected by the Curtius reaction. The acid **5** was nicely converted into its acid chloride **5a** with oxalyl chloride, whereas thionyl chloride proved decidedly less useful. The acid chloride was characterized by its amide **13**. Reaction of the acid chloride with activated sodium azide in benzene followed by treatment with ethanol gave the carbamate ester **14**, which was converted into the phthalimide **15** and subjected to hydrazinolysis. Subsequent reaction with hydrogen chloride in ether and isopropyl alcohol gave the amine hydrochloride **12**, isolated as a high-melting crystalline solid of high but not analytical purity.

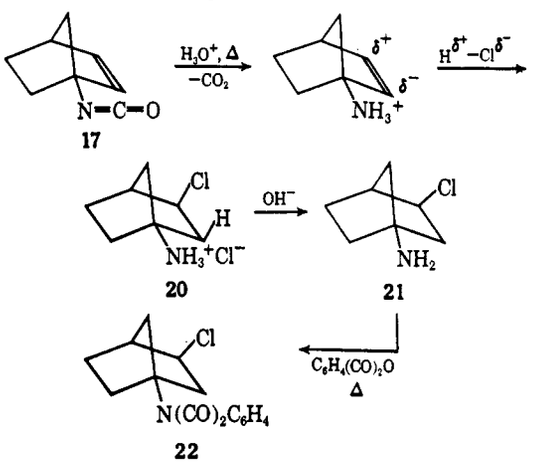


The structure of the amine salt **12** was established by spectra as well as by the catalytic hydrogenation of the phthalimide **15** to the known[18a] N-(1-norbornyl)-phthalimide (**16**). Alternatively, **5** could be smoothly converted into 1-norbornenyl isocyanate (**17**) by the Weinstock modification[20] of the Curtius reaction. In this method **5** was treated with ethyl chloroformate and triethylamine in aqueous acetone to produce the mixed anhydride. Subsequent direct reaction of this anhydride with sodium azide led to 1-norbornenylcarbonyl azide which was rearranged without isolation to **17** in hot toluene. Treatment of **17** with phenylmagnesium bromide readily afforded the benzamide **18**, analytically a better derivative of 1-norbornenylamine than was **12**. Another good derivative was the high-melting N,N′-di(1-norbornenyl)urea (**19**), which resulted when **17** was allowed to stand in moist solvents. Interestingly, if one used the alternative method of refluxing the intermediate isocyanate **17** with hydrochloric acid to obtain **12** directly, or if one allowed the amine salt **12** to stand in the hydrogen chloride, ether, and isopropyl alcohol mixture used in its preparation, addition of hydrogen chloride to the

(20) J. Weinstock, *J. Org. Chem.*, **26**, 3511 (1961).



norbornene double bond occurred and a product shown to be *exo*-3-chloro-1-norbornylamine hydrochloride (**20**) was isolated. The structure of **20** was deduced from the following facts. First, the molecular composition indicated that addition had occurred. Second, both the free amine **21** and its phthalimide derivative **22** were inert to alcoholic silver nitrate at 25°. As the *exo*-2-halo-1-norbornylamines are extremely rapid in this test,[15] the stated 3-chloro isomer was the logical alternative. Third, the appearance of the 3-proton centered at δ 3.97 in the nmr spectrum suggested its *endo* stereochemistry[21] and therefore the *exo* position of the chlorine. This reaction probably reflects the inductive influence of the 1-ammonium function on the orientation of ionic additions to the norbornene double bond. The effect of this substituent is in marked contrast to the effect of the 1-methyl function recently reported to be without much directive influence.[9b] There are other possible views, however, and further work is in progress in this area.[22] The chloro-

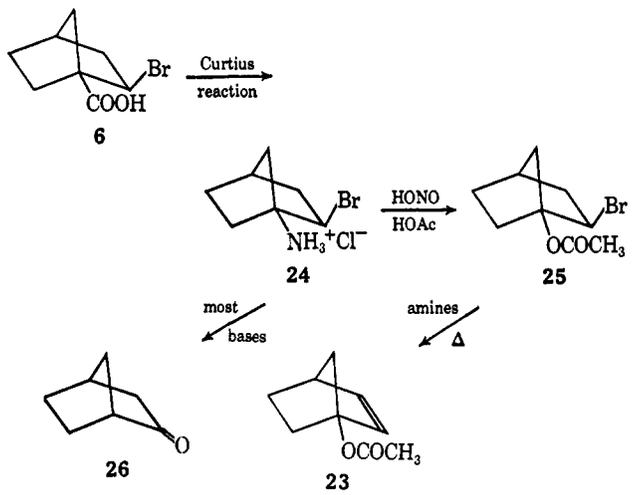


(21) In the past decade many studies have shown that *exo* protons are deshielded relative to *endo* protons. For examples in a series of epimeric bornane derivatives, see T. J. Flautt and W. F. Erman, *J. Am. Chem. Soc.*, **85**, 3212 (1963), where $\delta_{exo} - \delta_{endo} = 0.08$–$0.48$. We suggest that **21** (δ >CHCl 3.97) has a C-3 *endo* proton because *exo*-2-chlorobenzonorbornene (*endo* H at C-2) has δ >CHCl 3.8, while *endo*-2-chlorobenzonorbornene (*exo* H at C-2) has δ >CHCl 4.4: J. W. Wilt, G. Gutman, W. J. Ranus, Jr., and A. R. Zigman, *J. Org. Chem.*, **32**, 893 (1967). However, until the epimer of **21** is available, this structure must remain provisional.

(22) For instance, as the rate of addition is unknown relative to the rate of hydrolysis, a pathway involving the prior addition of hydrogen chloride to the double bond of the isocyanate ester **17** followed by hydrolysis to **20** must also be considered. However, the fact that **12** is itself convertible to **20** indicates that this alternative pathway is not necessary to explain the data. Other such additions are presently under study (with G. Miley).

amine salt **20** proved to be resistant to dehydrochlorination using potassium *t*-butoxide in *t*-butyl alcohol. Reaction under reflux for 6 hr gave only recovered **20**, again indicating that the chlorine could not be at an *exo*-2 position because *exo*-2-halo-1-norbornylamines give norcamphor rapidly under these conditions.[15]

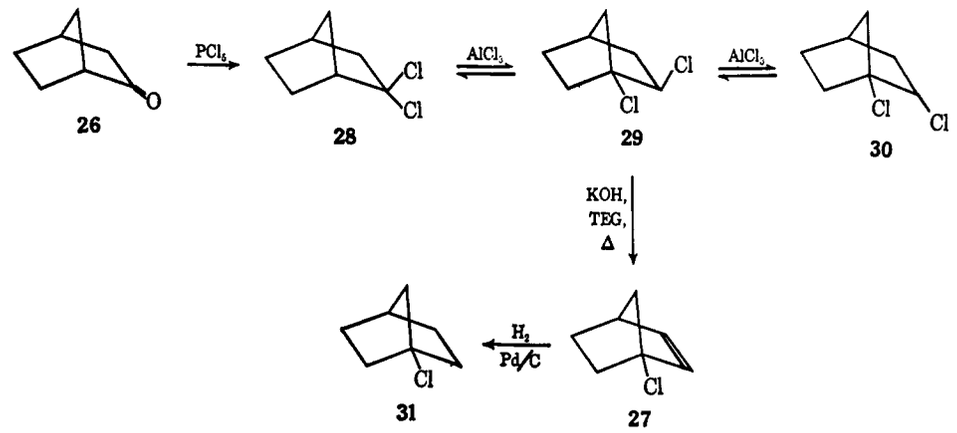
1-Norbornenyl acetate (**23**) has been previously made,[10] but the present synthesis has the advantages, we feel, of being operationally easier than that used before and of affording the ester free of isomers. The earlier synthesis involved a high-pressure reaction and extensive separation of isomers. The sequence used in the present study is illustrated. Because of its success



with acid **5**, the crucial conversion of the bromo acid **6** into the amine salt **24** was again achieved by the Curtius reaction. Deamination of the amine salt **24** in acetic acid led smoothly to *exo*-2-bromo-1-norbornyl acetate (**25**). Although nearly all attempts to dehydrobrominate this ester produced norcamphor (**26**) in high yield, one method involving the use of a mixture of *sym*-collidine and 3,5-lutidine as the base[23] proceeded rather well in the desired direction. The infrared spectrum of the resulting 1-norbornenyl acetate (**23**) was identical with that reported.[10] As **23** can be saponified without rearrangement, 1-norbornenol (**2**) can also be made in this way.

1-Norbornenyl chloride (**27**) was synthesized from norcamphor (**26**). As reported,[18] the ketone was converted into 2,2-dichloronorbornane (**28**) and then isomerized by means of aluminum chloride to a mixture of 1-*exo*-2- and 1-*endo*-2-dichloronorbornane, **29** and **30**, respectively. The isomerization produced an equilibrium mixture of *ca.* 20% **28**, 64% **29**, and 16% **30**. Dehydrochlorination of pure **29** (isolable from the isomerized mixture) in hot triethylene glycol with base led to the bridgehead chloride **27**, a colorless oil. Its structure was clearly demonstrated by hydrogenation to the known[18] solid 1-norbornyl chloride (**31**), as well as by the appearance of two vinyl protons centered at δ 5.89 and 6.02 and one bridgehead proton centered at δ 2.81 in its nmr spectrum. Its infrared spectrum had an intense absorption at 14.08 μ, due to C–H deformations characteristic of the unsubstituted norbornene double bond. The nmr spectrum presented an interesting example of shielding by neighboring chlorine. From the complex eight-line AB portion of an ABX multiplet at about δ 6, the following coupling constants could be extracted: J_{AB} = 5.6 cps, J_{AX} = 3.5 cps, and J_{BX} = *ca.* 1 cps. As the A proton was the more strongly coupled, it had to be the 3-proton, not the 2-proton as might have been anticipated because of the neighboring chlorine. We have observed this shielding by chlorine in 2-chloronorbornene and 2-chlorobenzonorbornadiene as well.[24] It is probably a reflection of the diamagnetic anisotropy of chlorine.[25]

Reactivity of 1-Norbornenyl Chloride.—1-Norbornyl chloride (**31**) is a classical example of inertness in nucleophilic displacement reactions.[26] 1-Norbornenyl chloride (**27**) proved to be equally adamant. Our various reaction attempts upon it involved solvolyses with the added promoters silver ion and lead ion. Neither reaction gave evidence of much chloride ion release even upon extended heating. A yield of 2.6% was obtained after 370 hr under reflux with alcoholic silver nitrate and no chloride ion was observed after 7 days in a sealed tube at 150° with lead acetate in aqueous dioxane. The chloride also failed to react with magnesium or lithium in a number of attempts. Phenyl azide gave a poor yield of adduct **32**[27] but 5,5-dimethoxy-1,2,3,4-tetrachlorocyclopentadiene afforded the adduct **33** nicely. Oxidation of **27** by air was readily apparent in older samples of the material. Hydrogen chloride was released and a polymeric material, aldehydic to some extent, formed. The



(23) H. H. Inhoffen, *et al.*, *Ann.*, **585**, 132 (1954).

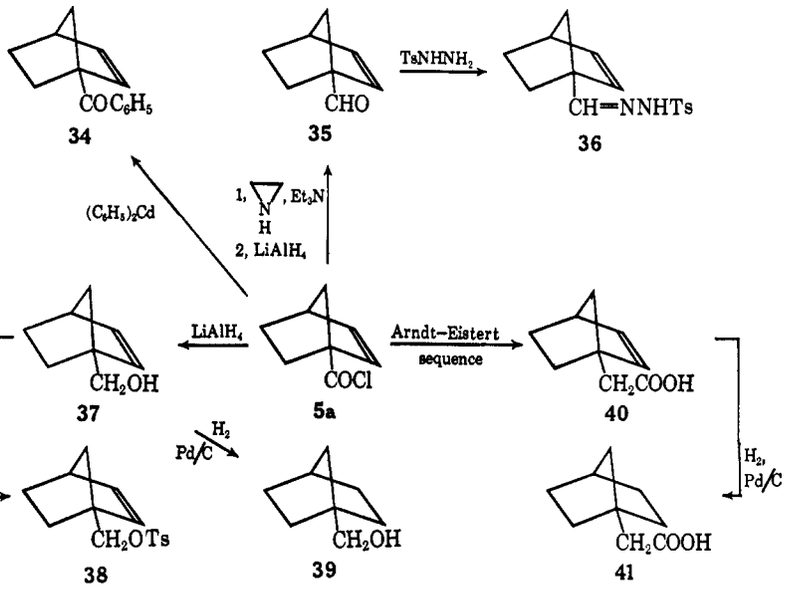
(24) J. W. Wilt, *et al.*, see ref 21.

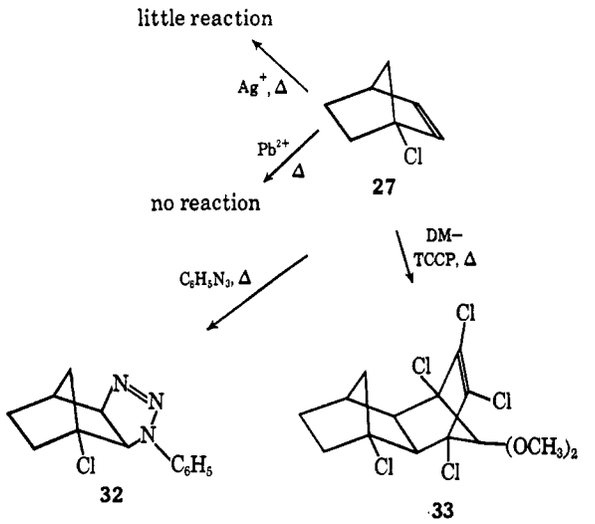
(25) G. S. Reddy and J. H. Goldstein, *J. Chem. Phys.*, **38**, 2736 (1963).

(26) For a recent review on bridgehead reactivity, see R. C. Fort, Jr., and P. von R. Schleyer, "Advances in Alicyclic Chemistry," Vol. 1, H. Hart and G. J. Karabatsos, Ed., Academic Press Inc., New York, N. Y., 1966, p 283 ff.

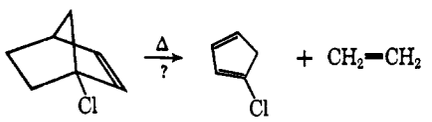
(27) The position of the phenyl group was not established. The structure given is favored by the polarity of the norbornene double bond and the probable character of the azide dipole.

SCHEME I

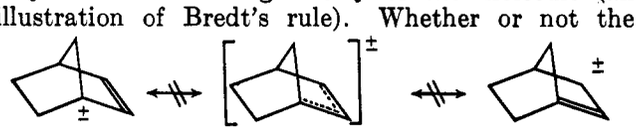




halide proved rather sensitive thermally, decomposing above 200° to two other substances by gas chromatography, possibly *via* a reverse Diels–Alder reaction as shown, though trapping techniques were ineffective at proving this point. The same behavior was noticed



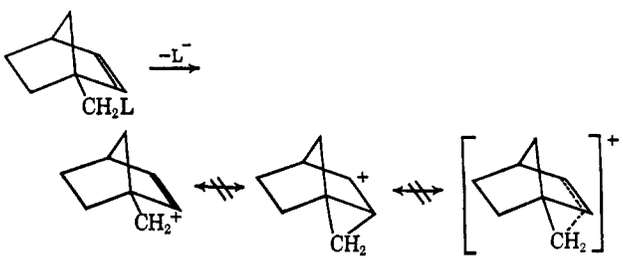
for 2-norbornenyl chloride (see Experimental Section). Although **27** is, by definition, an allylic chloride, it obviously possesses none of this kind of reactivity. Its bridgehead character dominates its chemistry (or lack of it) and little allylic delocalization can stabilize either cationic or anionic bridgehead sites, undoubtedly because of the geometry of the molecule (an illustration of Bredt's rule). Whether or not the



inductive effect of the double bond plays a significant role in the behavior of **27** is certainly not demonstrable by our studies to date.

II. Chemistry of Norbornenyl-1-carbinyl Derivatives. Syntheses.—Other transformations of acid **5** were achieved as illustrated. All of these reactions left a carbon function at the bridgehead (Scheme I). 1-Norbornenyl phenyl ketone (**34**) resulted, albeit in low yield, from the reaction of diphenylcadmium[28] on the acid chloride **5a**. Reduction of the acid chloride to the aldehyde was carried out *via* the N-acylaziridine.[29] The aprotic Bamford–Stevens reaction[30] of the tosylhydrazone **36**, one of the mechanistic studies done in the present work, is described later herein. The carbinol **37** was prepared by the reaction of lithium aluminum hydride with the acid chloride and thence converted into its tosylate **38**. A kinetic and product study of the hydrolysis of this tosylate is also described later. The catalytic reduction of carbinol **37** gave the previously known norbornyl-1-carbinol (**39**).[18] Finally, the Arndt–Eistert sequence proceeded normally and allowed a facile preparation of the homologous norbornenyl-1-acetic acid (**40**). This could be related to norbornyl-1-acetic acid (**41**), its saturated analog, by hydrogenation.

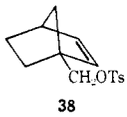
Hydrolysis of Norbornenyl-1-carbinyl Tosylate. Rate Studies.—It was next of interest to determine what effect the double bond would have on the rate of solvolysis of norbornenyl-1-carbinyl derivatives.[31] The system is actually homoallylic in structure, though the characteristic reactivity of such com-



(28) J. Cason, *Chem. Rev.*, **40**, 15 (1947).
(29) H. C. Brown and A. Tsukamoto, *J. Am. Chem. Soc.*, **83**, 2016, 4549 (1961).
(30) *Cf.* J. W. Wilt, C. A. Schneider, H. F. Dabek, Jr., J. F. Kraemer, and W. J. Wagner, *J. Org. Chem.*, **31**, 1543 (1966).
(31) Bly and co-workers independently have also investigated this point.[8]

pounds would not be expected because the geometry of the ring system allows little if any homoallylic delocalization.[32] So the difference in solvolytic reactivity found between, for example, tosylate **38** and its saturated analog, the known[18b] norbornyl-1-carbinyl tosylate (**42**), would represent a direct experimental measure of the inductive effect of the homoallylic double bond apart from its usually combined inductive plus resonance effects. Initial studies involved both acetolysis and formolysis of **38**, but the reactions were too complex. Serious drift in rate was noted in acetolysis, and addition of solvent to the double bond was especially troublesome in formolysis. The retardation of rate with time in acetolysis suggested considerable isomerization of **38** (presumably *via* ion-pair return) to a kinetically slower material. Independently, Bly and co-workers[8] found this same result in their study of the acetolysis of the brosylate of **37**. We decided to study hydrolysis instead and we changed to an aqueous acetone solvent and employed *sym*-collidine to neutralize the *p*-toluenesulfonic acid liberated in the reaction.[33] Without the collidine the reaction material colored badly and acetone aldol condensation products accumulated which affected the kinetics. Furthermore, one of the hydrolysis products, norbornenyl-1-carbinol (**37**), was destroyed by the sulfonic acid and solvent mixture (see later). When collidine was used, the reaction material stayed colorless, hydrolysis was cleanly first order, and product stability was demonstrable. The kinetic data are given in Table I.

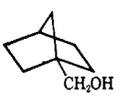
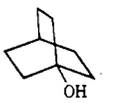
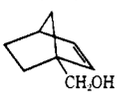
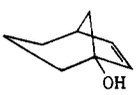
TABLE I
RATE DATA FOR THE HYDROLYSIS[a] OF TOSYLATES **42** AND **38**

Tosylate	$10^5 k_1$, sec^{-1}	ΔH^*, kcal/mole	ΔS^*, eu
	0.95 ± 0.05 (80.0°)[b]		
	2.39 ± 0.05 (90.0°)		
	5.76 ± 0.30 (100.0°)	23.0 ± 0.2	−0.02 ± 0.01
42			
	1.19 ± 0.07 (100.0°)		
	3.31 ± 0.08 (110.6°)		
	7.99 ± 0.44 (121.0°)	26.0 ± 0.2	−0.01 ± 0.01
38			

[a] In acetone–water (60:40 v/v) containing 0.03 *M* tosylate and 0.033 *M* *sym*-collidine. [b] Temperatures ±0.1°. Average of several experiments.

Product Studies.—For product isolation, the hydrolyses were performed on a larger scale and processed by gas chromatography. Runs were made with and without collidine. The various alcohol products were identified by comparison with authentic samples (except **44**, which is new). The composition of the product mixtures was determined by nmr spectroscopy. The results are collected in Table II. The change in product composition in the absence of collidine was checked by control studies. Of all the alcohols, only **37** was unstable under hydrolysis conditions with no collidine. It did not, however, rearrange to **44**, but rather it yielded an unknown product(s) that showed carbonyl properties. For this reason the yield of **44** was not very high (*ca.* 50%) under no-collidine conditions. Alcohol **43** was, however, a high-yield product (over 90%) under these conditions. With collidine present, the alcohol yields were very good (over 90%).

TABLE II
PRODUCT DATA FOR THE HYDROLYSIS OF TOSYLATES **42** AND **38**

Tosylate	Products, %		
			
42	**39**, [a] 8.5%	**43**, 91.5%; [a] 100%[b]	
			
38	**37**, [a] 42%	**44**, 58%; [a] 100%[b]	

[a] Product composition under conditions as in Table I, except that the hydrolyses were some fivefold larger in scale and were done at 113° for 48 hr. [b] Sole product isolated under conditions as in Table I, footnote *a*, *but no collidine present.*

While alcohols **39**[18] and **43** (1-bicyclo[2.2.2]octanol)[34] are known, bicyclo[3.2.1]oct-6-en-1-ol (**44**) has not been reported before. Its structure was originally assigned on the basis of spectral data. Both the infrared spectrum and the nmr spectrum indicated the compound was a tertiary alcohol. The former did not match that of 1-bicyclo[2.2.2]octenol (**45**). The nmr spectrum, however, indicated two vinyl protons centered at δ 5.76 and one bridgehead proton centered at δ 2.71, leading to structure **44** or to the Δ^3 isomer. As an example of the latter type of bicyclooctane, bicyclo[3.2.1]oct-2-ene has been reported[35] to have its vinyl protons strongly coupled (J = 9.5 cps). But no such splitting was observed in the hydrolysis product's spectrum and, moreover, an allylic resonance expected for a Δ^3 isomer's methylene group at C-2 (about δ 2) was absent. But apart from these spectral considerations, total support for the structure **44** came from the identity of our sample with that obtained by Bly.[8,36]

Discussion of Hydrolyses.—Three items interested us in the hydrolysis study. First, the retardation found in the unsaturated tosylate **38** amounted to *ca.* fivefold at 100°, which may be calculated to be *ca.* 16-fold at 25°, relative to the saturated analog **42**. Second, the extent of rearrangement during the hydrolysis was much less for **38** than for **42** and was sensitive, though to a decidedly different extent in each case, to the presence of the collidine. Third, the rearranged alcohol product found in each case differed in an interesting way, namely, ring expansion of the methano bridge in **42** to form the bicyclo[2.2.2]octyl derivative **43**, but ethano bridge migration in **38** to form the bicyclo[3.2.1]octenyl derivative **44**.

There have been many attempts to determine what solvolytic rate retardation would result from the

(32) M. Simonetta and S. Winstein, *J. Am. Chem. Soc.*, **76**, 18 (1954).

(33) Recently, urea has been successfully employed for this purpose in acetolysis by W. S. Trahanovsky, M. P. Doyle, and P. D. Bartlett, *J. Org. Chem.*, **32**, 150 (1967).

(34) C. A. Grob, M. Ohta, E. Renk, and A. Weiss, *Helv. Chim. Acta*, **41**, 1191 (1958).

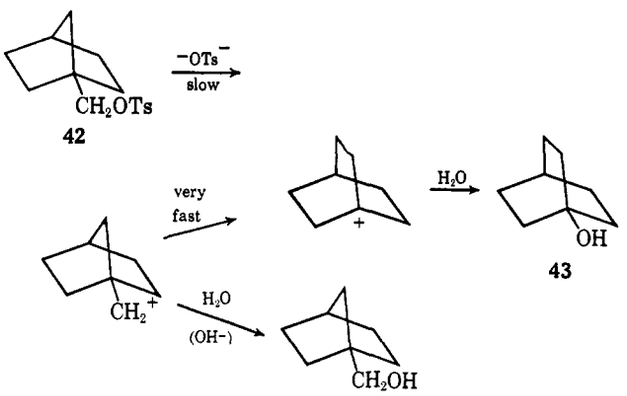
(35) R. R. Sauers and R. J. Tucker, *J. Org. Chem.*, **28**, 876 (1963).

(36) We are most grateful to Dr. Bly for the infrared and nmr spectra of **44**, as well as of the other two possible isomers, the Δ^2 and the Δ^4. Our sample was clearly **44** from the spectra. In addition, Bly has oxidized this solvolysis product to a cyclohexane derivative, thus eliminating the possibility of a Δ^2 or Δ^4 double bond (private communication).

purely inductive effect of a vinyl group.[37] The most common range of values is five- to tenfold for a homoallylically positioned (γ) double bond. But the subject is quite complex and the "answers" are dependent upon the approximations involved. One of the troubles in these determinations is the concomitant rate acceleration caused by participation of the double bond in solvolysis. In one study not complicated by this participation, Wilcox and Chibber[38] found the solvolytic rate ratio of saturated to δ-unsaturated substrates in 60% aqueous acetone to be fairly constant and to equal about 4 at 25° and about 2.5 at 100°, in good agreement with purely inductive rate retardation calculated by a Taft treatment. A movement of the double bond from the δ to the γ (homoallylic) position should increase the inductive effect by a factor of 2.8.[39] If this is so and if Wilcox's and our reactions are otherwise comparable, one concludes that our ratio (k_{42}/k_{38}) should be about 7 at 100° and about 12 at 25°, in reasonable agreement with those actually observed (5 and 16, respectively). We feel, however, that our *experimental* values are better measures of inductive retardation by the homoallylic double bond and that they may be of value in reinterpreting existing solvolytic data in this area.

On the basis of the above, then, the slower rate of hydrolysis of **38** seems well explained by an inductive effect of the norbornene double bond tightening the carbon-leaving group bond. Such an effect would be evidenced in the activation enthalpy primarily and indeed in the rate difference between the two tosylates nearly totally in this parameter (Table I). With regard to the inductive similarity between the vinyl and phenyl groups recently discussed by Bly,[37] it is perhaps relevant to mention that benzonorbornenyl-1-carbinyl tosylate (**4**, G = OTs), which we consider to be a model compound for the evaluation of the inductive effect of phenyl in homoallylic (neophyl-like in this case) compounds, is only about threefold slower than **38** in its rate of hydrolysis in 80% acetone at 130° in the presence of collidine.[13] Likewise, benzonorbornene-1-carboxylic acid (**3**, G = COOH) has a pK_A of 5.88 in 50% ethanol and is only 25% stronger an acid[17] than is **5**. It would indeed then appear that the two π systems, phenyl and vinyl, are quite comparable in their inductive effects in homoallylic structures.

The extent of rearrangement found for **42** in the present study, together with its known[18b,40] faster rate of acetolysis (seven- to eightfold) compared to neopentyl tosylate, might be viewed as evidence for some anchimeric participation by the methano bridge in its hydrolysis here. Neither observation *requires* participation for its explanation. As has been known for some time but recently cogently restated by Nordlander, *et al.*,[41] rearrangement can occur after the slow step and increased rates can be due to factors other than participation, *e.g.*, a higher ground-state energy or solvation effects. In the light of present knowledge of neopentyl systems in solvolysis,[41] very probably both the earlier acetolysis[18b,40] and the present hydrolysis of **42** involved slight, if any, anchimeric participation but rather a slightly enhanced unassisted ionization followed by rapid rearrangement. The high driving force for rearrangement



has been ascribed by Wiberg and Lowry[40] to relief of bond angle deformation, presumably the relief of the 96.7° C_1–C_7–C_4 methano bridge angle.[4] Their report mentioned the production of 1-bicyclo[2.2.2]-octyl acetate, contaminated slightly *via* infrared analysis with some (suggested) 1-bicyclo[3.2.1]octyl analog, as the acetolysis product. We never found ethano bridge migration with **42**, but when collidine was absent we did find rearrangement to the [2.2.2] alcohol **43** exclusively, in good agreement with Wiberg and Lowry. With collidine present, however, a modest amount of unrearranged **39** was also found (see Table II). This last result may be rationalized in that our solvent system (with collidine) is more nucleophilic than acetic acid[42] and the initially formed ion could be somewhat more easily captured by water or by hydroxide ion[43] before rearrangement. With no collidine present the formation of **39** by hydroxide ion is virtually precluded. Also, the solvent system is now less nucleophilic as the sulfonic acid liberated

(37) For a recent study with many references, see R. S. Bly and R. T. Swindell, *J. Org. Chem.*, **30**, 10 (1965).

(38) C. F. Wilcox, Jr. and S. S. Chibber, *ibid.*, **27**, 2332 (1962).

(39) R. W. Taft, Jr., "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p 592.

(40) K. B. Wiberg and B. R. Lowry, *J. Am. Chem. Soc.*, **85**, 3188 (1963).

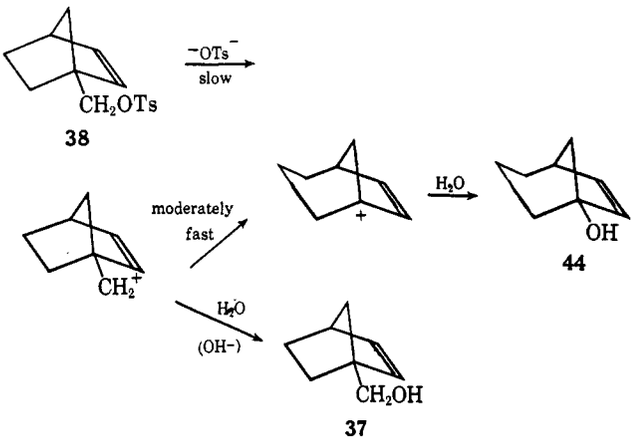
(41) J. E. Nordlander, S. P. Jindal, P. von R. Schleyer, R. C. Fort, Jr., J. J. Harper, and R. D. Nicholas, *ibid.*, **88**, 4475 (1966).

(42) This is perhaps most quantitatively expressed by the $d_1 - d_3$ (Δd) values of C. G. Swain, R. B. Mosely, and D. F. Brown, *ibid.*, **77**, 3731 (1955). These values are related to the nucleophilic vs. electrophilic properties of the solvent relative to 80% ethanol (Δd = 0.00), the larger the value the greater the nucleophilicity of the solvent. For 50% acetone, $\Delta d = -1.2$; for 90% acetone, Δd = 1.0; for acetic acid, $\Delta d = -7.9$. The presence of collidine would most assuredly raise the Δd value of our aqueous acetone solvent even more and keep, by removal of tosyl acid, Δd from decreasing as the hydrolysis progressed.

(43) Pure *sym*-collidine has $pK_A(25°)$ = 7.59 (H. C. Brown, S. Johnson, and H. Podall, *J. Am. Chem. Soc.*, **76**, 5556 (1954)) and, at the level used here, could produce a hydroxide ion concentration of about 10^{-6} *M*, sufficiently high to capture a cationic intermediate, but too low to effect any significant S$_N$2 attack on **42**. An S$_N$2 process by collidine itself is less likely. This may be seen by noting that the closely related bicyclo[2.2.2]octyl-1-carbinyl and bicyclo[2.2.2]oct-2-enyl-1-carbinyl tosylates undergo S$_N$2 attack by thiophenolate ion in ethanol at 75.3° with $k_2 = 22 \times 10^{-5}$ and 45.1×10^{-5} l. mole^{-1} sec^{-1}, respectively: H. D. Holtz and L. M. Stock, *ibid.*, **87**, 2404 (1965). However, the nucleophilic strength of *sym*-collidine is *ca.* 4×10^{-6} that of thiophenolate ion, shown as follows. The nucleophilicity of pyridine is 4×10^{-5} that of thiophenolate ion (R. Breslow, "Organic Reaction Mechanisms," W. A. Benjamin, Inc., New York, N. Y., 1965, p 78) and *sym*-collidine is a tenfold weaker nucleophile than pyridine: H. C. Brown, D. Gintis, and H. Podall, *J. Am. Chem. Soc.*, **78**, 5375 (1956). One can, therefore, calculate that the S$_N$2 attack of *sym*-collidine on **38** and **42** would have $k_2 = 10^{-9}$ l. mole^{-1} sec^{-1}, some 10^3 to 10^4 times slower than the hydrolysis rate constant. Furthermore, such an attack should be reflected in the rate constant, but increasing the collidine concentration in the analogous hydrolysis of the closely related benzonorbornenyl-1-carbinyl tosylate (**4**, G = −OTs) in fact slightly *decreased* the hydrolysis rate constant, presumably by a solvent effect (H. Dabek, Jr., unpublished work).

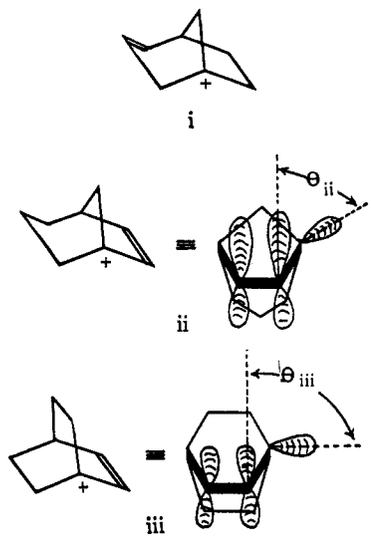
would attenuate this property. So the complete rearrangement found is understandable. The formation of **43** exclusively under these conditions will be discussed later in conjunction with the products from **38**.

The reduced solvolytic rate for **38** arose in our view from the previously postulated strengthening of the carbon–tosylate bond by the inductive effect of the double bond. But the difference in the extent of rearrangement and the type of bicyclic rearranged product observed in the two tosylates required a more involved explanation. Because much more (nearly half) of the product was not rearranged from **38**, one might suggest that it underwent considerably more SN2 attack (by hydroxide ion or by collidine) than did **42**. But the two tosylates would not be expected to differ this much in SN2 reactivity (compare their homologs studied by Holtz and Stock[43]), so this is not a good explanation. Rather, it is more likely that rearrangement again occurred in the product-determining portion of the process. In the case of **38**, however, rearrangement faced stiff competition from nonrearrangement, as shown, whereas rearrangement greatly predominated in the case of **42**. If this is so,



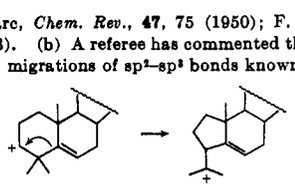
then it is clear that the rearrangements of the parent ions from **42** and **38** differ in rate, the former being faster. Most certainly both the rearrangements are exothermic, but the transition state is probably reached earlier and the activated complex more resembles the reactant in the case of **42** than in the case of **38**.[44] Thus the strain present in the initial ion (*i.e.*, that due to the methano bridge) determined the reaction course for **42**, giving rise to the product **43** because this strain was better relieved in this way. Because the transition state (in our postulate) was reached early, the relative energies of the two possible bicyclic product ions played a minor role here. Had product ion stability been important, considerable 1-bicyclo[3.2.1]octanol should have accompanied **43**, as their bridgehead cationic precursors have comparable stability.[26] But in **38** the methano bridge angle, C_1–C_7–C_4, is now wider because of the double bond present which stretches the boat cyclohexene ring and flattens the bridge angle.[45] This reduces the driving force for methano bridge migration and allows the activated complex, reached in a later transition state, to reflect the properties of the product to a greater degree.

Three bicyclic ions are possible by rearrangement in this case, ions i, ii, and iii. But they are not equally likely. To begin with, the probable migrating groups are the methano and/or the ethano bridges, but not the etheno bridge because of the hybridization of the migrating atom in this case. The sp^3–sp^2 hybridization present in the C_1–C_2 bond in **38** would have two contramigratory effects. First, it should tighten the bond: $D(CH_3\text{–}X)$, X = $-CH_2CH_3$, 82 kcal/mole; X = $-CH{=}CH_2$, 109 kcal/mole.[46a] Second, it should cause a bond moment unfavorable toward dispersal of positive charge from the carbinyl carbon to C_1 during migration of the C_1–C_2 σ bond to form ion i. Both effects would reduce the migration ability of this σ linkage.[46b] So ions ii and/or iii become more probable. Of these two, framework molecular orbital (FMO) models indicate (see drawings) that the 1-bicyclo-[3.2.1]octenyl cation (ii) leading to product **44** is capable of some allylic stabilization ($\theta_{ii} \cong 60°$), while the 1-bicyclo[2.2.2]octenyl cation (iii) that would lead to

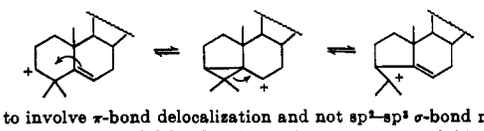


(44) G. S. Hammond, *J. Am. Chem. Soc.*, **77**, 334 (1955).
(45) P. von R. Schleyer and R. D. Nicholas, *ibid.*, **83**, 182 (1961).

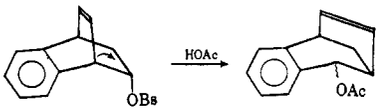
(46) (a) M. Szwarc, *Chem. Rev.*, **47**, 75 (1950); F. H. Field, *J. Chem. Phys.*, **21**, 1506 (1953). (b) A referee has commented that, on the contrary, there are many such migrations of sp^2–sp^3 bonds known, *e.g.*



This is not the prevalent view of such transformations: B. Capon, *Quart. Rev.* (London), **18**, 96 (1964). Rather, each of the above ions is held to be either in rapid equilibrium with a third, as shown, or to be a canonical form of a single delocalized species. In any case this i-steroid type rearrangement is



believed to involve π-bond delocalization and not sp^2–sp^3 σ-bond migration. Prevention of such π-bond delocalization is the very essence of this investigation. We feel that for the etheno bridge to migrate in **38**, a real *σ-bond migration* is required and that the above π-bond delocalization is very improbable in this case because of the geometry of the ring. It must be added that the rearrangement shown, recently reported by H. Tanida,



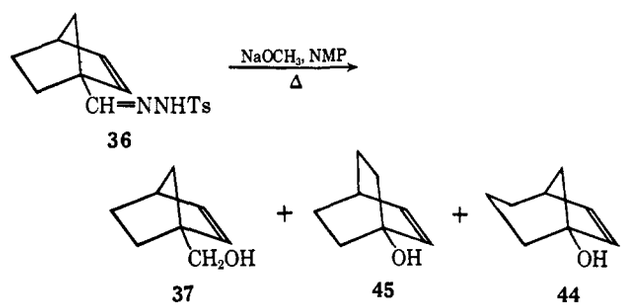
K. Tori, and K. Kitahanoki, *J. Am. Chem. Soc.*, **89**, 3212 (1967), is claimed to be a real sp^2–sp^3 σ-bond migration, and not π-bond delocalization. However, in this case a benzylic product ion is formed and the σ-bond migration could be eased by this fact.

product **45** is not ($\theta_{iii} = 90°$).[47] Clearly ion i has no possibility of allylic stabilization either.

The conclusion may be drawn, then, that ion ii is more probable than ion i and more stable than ion iii. Both these factors could be reflected in the formation of the activated complex during rearrangement and lead to alcohol **44** rather than its isomers.

Although the [3.2.1] product was again the major one (57%), Bly and co-workers[8] reported that 1-bicyclo[2.2.2]octenyl acetate (4%) did result in the acetolysis of the brosylate of **39**.[48] We rationalize this result once more by viewing the activated complex reached during rearrangement. In acetic acid the initially formed cation from the arenesulfonate probably rearranged as an ion pair, or at least without benefit of much solvation in this poorly ion-solvating medium. The activated complex was therefore formed early and little resembled the product(s). So the considerations above that made ion ii a better product choice than ion iii become less important and allow some of the alternative reaction path to be followed. Moreover, Bly found only 20% unrearranged material compared to our 42%. Again this is, in our view, a reflection of an earlier transition state for acetolytic rearrangement, just as discussed above for the hydrolytic rearrangement of **42**. It is noteworthy that product from the mechanistically improbable ion i was not found in either Bly's or our study.

"Aprotic" Bamford–Stevens Reaction of Norbornene-1-carboxaldehyde Tosylhydrazone (36).—A different approach to cationic rearrangements, particularly in bicycloalkyl-1-carbinyl derivatives, is to decompose aldehyde tosylhydrazones with base in N-methyl-2-pyrrolidone (NMP).[30] This process involves the formation of diazoalkanes, which are then protonated by the parent tosylhydrazones. Subsequent reactions of the diazonium ions so formed reflect the rearrangement tendencies of the carbon system, often leading to sulfinic esters *via* reaction with the *p*-toluenesulfinate ion present and undergoing cleavage by the NMP solvent to afford alcohols. Though the cleavage is without rearrangement, the product alcohols are often rearranged because of prior rearrangement of the cationic intermediates before capture by the sulfinate ion.[49] Several different bicyclic compounds had been studied in this laboratory earlier, among them the norbornyl-1-carbinyl example. It was therefore of interest to see what effect the double bond in the norbornenyl-1-carbinyl analog would have on this particular mode of rearrangement. Reaction of tosylhydrazone **36** with sodium methoxide in NMP at 180° led to a mixture of alcohols, isolated in low yield by gas chromatography. The composition of the mixture was best established by nmr spectroscopy, which showed *ca.* 47% of **44**, 44% of **45**, and 9% of **37**. Other products included the expected sulfur-containing by-products, *p*-tolyl *p*-toluenethiolsulfonate and bis-*p*-tolyl disulfide. The interesting aspect of this reaction is the appearance of 1-bicyclo[2.2.2]octenol (**45**) as a major component of the product mixture. The methano bridge had not been observed to migrate in the hydrolysis of tosylate **38** (see earlier) and the fact that it did so in this reaction deserves comment.



First, Bly and co-workers[8] had observed little ring expansion (4%) to the acetate of **45** in their study of the acetolysis of norbornenyl-1-carbinyl brosylate at 100°, but upon deamination of norbornenyl-1-carbinylamine in acetic acid they observed much more expansion of this type (31%), even at 20°. It is well known[50] that cationic species produced in deaminations are considerably more energetic than those formed in solvolyses and that major differences exist in the type and extent of rearrangement found in each case. Commonly, those rearrangements that are minor in solvolysis take on greater importance in deamination, presumably because of the higher energy content in the product-forming ion (either diazonium or carbonium). These rearrangements during deamination are therefore faster and, again in our view, their activated complexes resemble the reactants to a greater degree than those encountered in solvolysis. Accordingly, this serves adequately to explain the present results. In the hydrolysis of tosylate **38** the methano bridge did not migrate because of its decreased steric strain, allowing the transition state to be reached later and favoring the formation of **44** because of the allylic delocalization possible in ion ii formed by the alternative ethano bridge migration. But in the tosylhydrazone decomposition, which bears a mechanistic similarity to deamination in that diazonium ions are intermediates, the transition state is now reached earlier and the energetic favorability of ion ii over ion iii becomes less important. So the two pathways are expected to compete much more evenly and perhaps even statistically, as shown. The nearly equal formation of **44** and **45** supports this view. Likewise, the grossly increased extent of rearrangement here (91%) compared to hydrolysis (58%) also implicates an earlier transition state in the reaction of **36**.

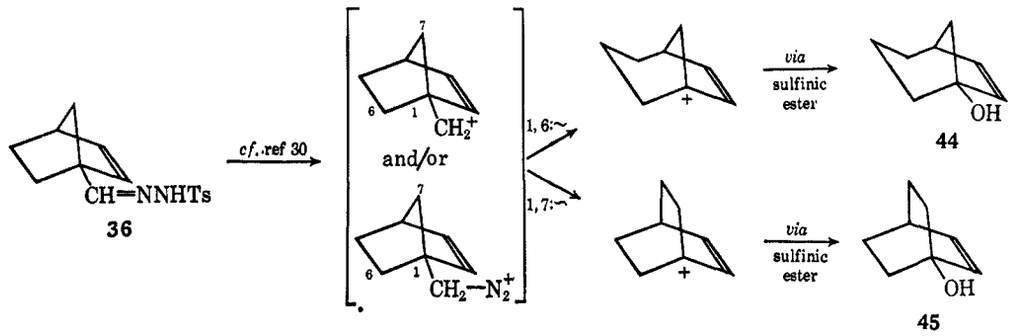
Further work on other aspects of the chemistry of 1-norbornenyl and norbornenyl-1-carbinyl derivatives is in progress. We hope to communicate the results of this later work in other papers of this series.

(47) The π-electron stabilization of ii compared to iii (neglecting strain differences) can be approached by simple Hückel theory. Ion ii has $\theta_{ii} \cong 60°$, therefore $S_{1,7} = {}^1/_2 S_{8,7}$ and $\beta_{1,7} = 0.56\beta_{8,7}$, giving energy levels in ii $= \alpha + 1.14\beta$, α, and $\alpha - 1.14\beta$. Ion iii has $\theta_{iii} = 90°$, therefore $S_{1,2} = 0$ and $\beta_{1,2} = 0$, giving energy levels in iii $= \alpha + \beta$, α, and $\alpha - \beta$. The populated orbitals in ii and iii differ then by 0.28β. If β is taken as 18 kcal/mole, then ii is more stable by about 5 kcal/mole. This kind of calculation may be found in J. D. Roberts, "Molecular Orbital Calculations," W. A. Benjamin, Inc., New York, N. Y., 1961, p 82 ff.

(48) In ref 8a there appears to be a reversal of Bly's products **3** and **4** in the structural formulas.

(49) J. W. Wilt, R. G. Stein, and W. J. Wagner, *J. Org. Chem.*, **32**, 2097 (1967).

(50) See ref 3, pp 205–213.



Experimental Section

Melting points and boiling points are uncorrected for stem exposure. The former were taken on a calibrated Fisher-Johns block or in sealed tubes (s.t.) in an oil bath. Only significant infrared absorptions are given (in microns) and the spectra were determined on Perkin-Elmer Model 21 or Beckman IR-5a instruments. Ultraviolet spectra were obtained on a Beckman DK-2 spectrophotometer. Nuclear magnetic resonance (nmr) spectra were obtained on Varian A-60 or A-60A spectrometers with tetramethylsilane as the internal standard. Samples were normally about 10% solutions in deuteriochloroform or carbon tetrachloride. The resonance values are in parts per million (δ units) and, for the case of most multiplets, are the centers, not the true chemical shifts. Integrations were in agreement with the structures given and the relevant proton is italicized when pertinent. The symbols used for the appearance of the signals are: s, singlet; d, doublet; t, triplet; q, quartet or doubled doublet; and m, multiplet. At times higher order splitting was apparent but the symbols used refer to the gross shape of the signal. Gas–liquid partition chromatography (glpc) was performed on Aerograph A-90-P and Nester-Faust Anacro 1A instruments using helium at 60 ml/min as the carrier gas. Microanalyses were done by Micro-Tech Laboratories, Inc., Skokie, Ill., and by Galbraith Laboratories, Inc., Knoxville, Tenn. Only representative procedures are given in those instances where many preparations were carried out.

Dehydrobromination of *exo*-2-Bromonorbornane-1-carboxylic Acid (6) with Excess Base.—Acid **6**[14a] (16.4 g, 0.075 mole) was added with efficient stirring to a refluxing solution of potassium *t*-butoxide (0.185 mole) in *t*-butyl alcohol (150 ml). After the addition, heating and stirring were continued for 12 hr. Water (200 ml) was then added cautiously, followed by concentrated hydrochloric acid until the solution was acidic to congo red paper. The material was thoroughly extracted with ether and the extracts were dried and distilled. The product was a foul-smelling mixture of acids, 9.3 g, 87.7%, bp 125–135° (4 mm), that was processed as follows. The product (1.38 g, 10 mmoles) was methylated by diazomethane and analyzed by glpc (neopentyl glycol disuccinate, 160°). Two esters eluted, each of which was collected and identified, in the one case as **methyl norbornene-1-carboxylate** (**9**, 28.5%) and in the other case as **methyl norbornene-2-carboxylate** (71.5%). The identifications were by spectral and glpc comparison with the authentic samples described below. Also, hydrogenation of the above mixture of unsaturated acids (Pd/C, 40 psig H_2, 25°) proceeded readily to a mixture of saturated acids (neut equiv: calcd, 140.3; found, 142.4). These acids were subsequently methylated and analyzed *via* glpc as above to afford the methyl esters of norbornane-1- and norbornane-2- (principally *endo*) carboxylic acids in percentages close to those given above. Again identification of the saturated methyl esters was achieved by spectral and glpc comparison with authentic samples.

Dehydrobromination of Acid 6 with an Equivalent of Base. Norbornene-2-carboxylic Acid (7).—Acid **6** (22 g, 0.1 mole) was added in one portion to a solution of potassium *t*-butoxide (0.1 mole) in *t*-butyl alcohol (250 ml) at 15°. The solution was then heated at reflux for 2 days during which it was protected from moisture. After the volume was reduced to about one-tenth the original by distillation of the solvent, ether (200 ml) was added and the mixture was extracted with water (three 75-ml portions). The ether phase was then shaken well with saturated aqueous sodium carbonate (200 ml). The alkaline solutions were combined, strongly acidified, and reextracted with several portions of ether. Upon evaporation of the dried ether extracts, crude norbornene-2-carboxylic acid (**7**, *ca.* 14 g, quantitative yield) was obtained as a viscous oil that could be distilled at 125–127° (3.2 mm), but with great loss due to apparent polymerization. The center cut, 7.5 g, bp 126° (3.2 mm) (lit.[19] mp 21.5–22.5°, bp 96° (0.6 mm)), was then characterized: λ^{neat} 5.94 (C=O, conjugated), 6.24 (>C=C<); δ^{CDCl_3} 10.3 s (COOH), 7.1 d (>C=CH–), 3.25 m, 3.05 m (bridgehead H's), 2.50–0.90 m (other ring H's); neut equiv, calcd 138, found 145.

The acid was analyzed as its **S-benzylisothiuronium salt** (recrystallized once from dioxane, mp 170–172°).

Anal. Calcd for $C_{16}H_{20}O_2N_2S$: C, 63.13; H, 6.62. Found: C, 62.82; H, 6.67.

The ethyl ester of **7** was prepared from the acid and ethanol using boron trifluoride etherate as catalyst: yield, 60%; bp 73–75° (1.4 mm); λ_{alc}^{max} 227.5 mμ. The infrared spectrum of the ester was identical with that of another sample.[51] A small sample of **methyl norbornene-2-carboxylate** was similarly prepared and purified by preparative glpc (neopentyl glycol disuccinate, 180°) as a colorless oil: λ^{neat} 5.80 (C=O), 6.25 (>C=C<); δ^{CCl_4} 6.8 d (–CH=C<), 3.23, 3.0 m (bridgehead H's), 3.63 s (OCH_3), 2.0–1.0 m (other ring H's). These data compare favorable with those reported.[19]

Anal. Calcd for $C_9H_{12}O_2$: C, 71.02; H, 7.95. Found: C, 70.81; H, 8.16.

This ester was the same as the major methyl ester produced from **6** *via* dehydrobromination followed by treatment with diazomethane (see earlier). On standing over a period of months the ester thickened considerably.

Methyl *exo*-2-Bromonorbornane-1-carboxylate (8).—A mixture of acid **6** (the acid must be pure, mp over 147° for best results, 180.9 g, 0.826 mole) and potassium carbonate (anhydrous, 129 g, 0.934 mole) was placed into acetone (850 ml). The resulting paste was heated to reflux and stirred as dimethyl sulfate (89 ml, 0.934 mole) was added in portions. After 6 hr of heating, the mixture was cooled and filtered from the potassium sulfate, which was washed thoroughly with acetone. These washings were added to the previous bulk filtrate, which was concentrated on a rotary evaporator. The oily residue was taken up in ether, washed three times with 10% aqueous sodium carbonate and then water, dried, and finally distilled to afford ester **8** as a colorless oil: yield, 176 g (91.5%); bp 103.4–104° (4.5 mm), 115–121° (11 mm); $n^{25}D$ 1.5056 (lit.[14] bp 117–118° (5 mm), $n^{25}D$ 1.5055); λ^{neat} 5.75 (C=O); δ^{CCl_4} 4.15 m (>CHBr), 3.67 s ($COOCH_3$), 2.5–1.0 m (other ring H's). This preparation is considerably faster, easier, and less dangerous on the scale used than the earlier method using diazomethane.[14] Also, the present yield is somewhat better, as we obtained the ester in 83.5% yield using diazomethane.

Norbornene-1-carboxylic Acid (5).—The methyl ester **8** (25.7 g, 0.11 mole) was added in one portion to a freshly made solution of potassium *t*-butoxide (0.25 mole) in dry *t*-butyl alcohol. The solution was then refluxed for 3 hr, at which time water (10 ml) was added and the heating continued for another 72 hr. Further water (35 ml) was added and the solvent was distilled off (100 ml total) until the temperature of the material reached *ca.* 100°. The caustic residue was chilled, extracted once with ether to remove some oily material, and then strongly acidified with concentrated hydrochloric acid. The precipitated material was collected and recrystallized from water to yield fine needles of colorless norbornene-1-carboxylic acid (**5**):

(51) We thank Dr. N. Pappas of the DuPont Co. for the infrared spectrum and other data on this ester: bp 85–87° (5.2 mm); λ_{alc}^{max} 230 mμ. See P. J. Graham, E. L. Buhle, and N. Pappas, *J. Org. Chem.*, **26**, 4658 (1961).

yield, 12.1 g (90%); mp 95–96° (though particular samples often had mp 90–91°); λ^{KBr} 5.85 (C=O), unconjugated, 6.33 weak (>C=C<), 14.2 (*cis* -CH=CH-); δ^{CDCl_3} 9.27 s (COOH), 6.2 m (-CH=CH-), 3.0 m (bridgehead H), 2.17–1.17 m (other ring H's).

Anal. Calcd for $C_8H_{10}O_2$: C, 69.55; H, 7.29. Found: C, 69.45; H, 7.03.

The **S-benzylisothiuronium salt** was prepared in the usual way and recrystallized once from dioxane, mp 172.5–174°.

Anal. Calcd for $C_{16}H_{20}O_2N_2S$: C, 63.13; H, 6.62. Found: C, 62.94; H, 6.72.

The **phenacyl ester,** a white micaceous solid from ethanol, was prepared in routine fashion, mp 69–70.5°.

Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 74.78; H, 6.24.

A small sample of **5** was hydrogenated (Pd/C, 1 atm, 25°) in sodium hydroxide solution. Isolation of the product afforded **norbornane-1-carboxylic acid (11)**: mp 111–112° (lit.[14,18] 111–112°, 113.8–115.5°). All spectra of the material were identical with those of the authentic acid, prepared as described.[14]

Methyl Norbornene-1-carboxylate (9).—Treatment of acid **5** with diazomethane in the normal manner gave the colorless methyl ester, **9**: yield, 85%; bp 48–49° (0.15 mm); λ^{neat} 5.78 (C=O), 6.36 weak (>C=C<), 14.1 (*cis* -CH=CH-); δ^{CCl_4} 6.1 m (-CH=CH-), 3.71 s ($COOCH_3$), 2.97 m (bridgehead H), 2.0–1.0 m (other ring H's).

Anal. Calcd for $C_9H_{12}O_2$: C, 71.02; H, 7.95. Found: C, 70.73; H, 8.01.

This ester could be prepared directly from ester **8** by treatment with N,N-dimethylaniline under reflux for 12 hr. The yield was only 29.4%, however, and other reactions occurred, so this is not considered a good alternative to the synthesis described. Some **9** was also produced from **8** by simply distilling the latter at atmospheric pressure. But here, too, other products formed and the method is not considered preparatively useful. Ester **9** was the same as the minor methyl ester produced from acid **6** *via* dehydrobromination followed by treatment with diazomethane (see earlier).

Ester **9** could be detected in the reaction of the bromo ester **8** with potassium *t*-butoxide described above, but mostly ***t*-butyl norbornene-1-carboxylate (10)** was formed in the reaction. The ester was isolable from the reaction by avoiding the addition of water and the subsequent saponification. Ether extraction of the ester from the pasty residue remaining after the removal of the solvent and eventual distillation gave the ester as a colorless, pleasant-smelling oil: yield, 65%; bp 88–90° (*ca.* 11 mm); λ^{neat} 5.77 (C=O), 6.34 weak (>C=C<), 7.18, 7.32, both strong (*t*-butyl), 14.01 (*cis* -CH=CH-); δ^{CCl_4} 6.0 m (-CH=CH-), 2.9 m (bridgehead H), 2.1–1.0 m (other ring H's) 1.43 s (*t*-butyl).

Norbornene-1-carboxylic Acid Chloride (5a).—While this acid chloride was prepared in the usual way with thionyl chloride (44% yield), an increased yield was realized by the use of oxalyl chloride. The acid chloride was obtained as a colorless oil: yield, 87.6%; bp 58–59° (5.8 mm). Hydrolysis of **5a** regenerated acid **5** quantitatively. The acid chloride was used directly in further work.

Norbornene-1-carboxamide (13).—The acid chloride above (*ca.* 0.5 ml) was dissolved in dry ether and ammonia gas was passed into the solution. The white solid that formed was extracted with hot benzene in a Soxhlet apparatus overnight. The benzene was evaporated and the solid residue was recrystallized from hot water and then from benzene. The amide formed snowlike platelets: sintered from 187°; mp 199–201° dec (205–208° in s.t.); λ^{KBr} 2.92, 3.08, 5.98, 6.12, all strong ($CONH_2$), 6.33 weak (>C=C<), 14.15 (*cis* -CH=CH-).

Anal. Calcd for $C_8H_{11}ON$: C, 70.07; H, 8.08. Found: C, 69.96; H, 7.84.

The amide could be converted into a nitrile (λ^{neat} 4.45) upon distillation from phosphorus pentoxide or thionyl chloride.

Ethyl N-(1-Norbornenyl)carbamate (14).—Sodium azide (activated, 7.4 g) was added to the acid chloride **5a** (17.7 g, 0.113 mole) in dry benzene (50 ml) and refluxed with stirring for 20 hr. The odor of the acid chloride persisted, so 1 g more of sodium azide was added and the stirring was continued for another 23 hr. While the mixture was heated in a hot water bath, absolute ethanol (20 ml) was added dropwise. Some hydrogen chloride fumes were noticed. After 3 hr, the solution was allowed to stand overnight. The red solution was washed twice with water to remove inorganic salts and then dried over sodium sulfate. Vacuum distillation gave three fractions: **ethyl norbornene-1-carboxylate** (7.96 g, 42%, bp 58° (2.3 mm)); an intermediate fraction containing the ethyl ester and the carbamate (0.98 g, *ca.* 10%, bp 62–73° (0.4 mm)); and colorless carbamate ester **14** (6.63 g, 32% based on initial acid chloride, bp 82° (0.5 mm), $n^{25}D$ 1.4852, d_{27}^{27} 1.015).

Anal. Calcd for $C_{10}H_{15}O_2N$: C, 66.27; H, 8.34. Found: C, 65.87; H, 8.25.

The material colored on standing so spectral data was taken quickly: λ^{neat} 2.95 (NH), 5.80 (C=O), 14.0 (*cis* -CH=CH-); δ^{CCl_4} 6.1 m (-CH=CH-), 5.5 m (NH), 4.13 q ($-OCH_2CH_3$), 2.81 m (bridgehead H), 2.0–1.0 m (other ring H's), 1.23 t ($-CH_2CH_3$).

N-(1-Norbornenyl)phthalimide (15).—Ester **14** (4.3 g, 0.024 moles) and phthalic anhydride (6.9 g) were placed into a test tube and heated in an oil bath at 210–230° for 45 min. The black melt was cooled, dissolved in ethanol, and poured into a large volume of 10% aqueous sodium bicarbonate. The separated solid was collected and recrystallized from ethanol several times with the use of decolorizing carbon. The phthalimide **15** was an offwhite crystalline solid: yield, 3.31 g (63%); mp 109.5–110°; λ^{KBr} 5.61 and 5.80 (imide ring C=O); δ^{CCl_4} 7.81 m (ArH), 6.66 d (C-2 vinyl H, J_{AB} = 7 cps), 6.2 q (C-3 vinyl H, J_{BX} = 3 cps), 2.95 m (bridgehead H), 2.15–1.77 m (other ring H's).

Anal. Calcd for $C_{15}H_{13}O_2N$: C, 75.29; H, 5.48. Found: C, 75.03; H, 5.50.

The phthalimide **15** was reduced in ethanol upon treatment with hydrogen and palladium on charcoal to give white, crystalline **N-(1-norbornyl)phthalimide (16)**, mp 99.5° (lit.[18a] mp 101.5–102.5°), in high yield.

1-Norbornenylamine Hydrochloride (12).—The above phthalimide **15** (1.74 g, 7.3 mmoles), hydrazine (64%, 1.4 ml), water (0.6 ml), and ethanol (95%, 31 ml) were refluxed for 2 hr. Concentrated hydrochloric acid (10 ml) was then added and the mixture was filtered to remove phthalhydrazide, which was washed well with water, and the washes were added to the acidic filtrate. After evaporation to dryness, the residual solid was digested in an ethanol–ethyl acetate solution on a steam bath and filtered, and the filtrate was made basic with sodium hydroxide solution (10%). The mixture was then extracted twice with 15-ml portions of ether. To the combined extracts was added isopropyl alcohol saturated with hydrogen chloride. The amine hydrochloride **12** precipitated as a white, microcrystalline solid: yield, 0.51 g (48.1%); mp over 300°; λ^{KBr} 3.35 broad, 3.8, 3.9, 3.97, 4.82, 6.17, 6.62 (all indicate $-NH_3^+$), 6.3 weak (>C=C<), 14.0 (*cis* -CH=CH-). The analysis indicated, however, that the salt was not pure.

Anal. Calcd for $C_7H_{12}ClN$: C, 57.73; H, 8.31. Found: C, 56.92; H, 8.06.

Moreover, on some occasions little **12** precipitated using this procedure. The preparation was very sensitive to the amount of solvent used and its hydrogen chloride content. It could not be made reliably reproducible.

The mother liquor, when evaporated, afforded largely the chloroamine salt **20** (see following), identified by infrared and nmr comparison with **20** made as later described. It is therefore probable that **20** was the impurity in **12** as made above and the nonreproducible nature of the process was attributed to the variable occurrence of this side reaction of addition to the double bond.

N-(1-Norbornenyl)benzamide (18).—To obtain a better derivative of 1-norbornenylamine, the conversion of acid **5** to 1-norbornenyl isocyanate (**17**) was achieved by the method of Weinstock.[20] Acid **5** (11.9 g, 0.086 mole) was treated with triethylamine (10.2 g, 0.1 mole) in an aqueous system containing sufficient acetone to dissolve all the reactants. At 0°, ethyl chloroformate (12.5 g, 0.11 mole) was added dropwise and the resulting mixture was stirred for 30 min at 0°. Sodium azide (8.6 g, 0.13 mole) in water was then added at a rate such that the temperature remained around 0° and the mixture was then stirred for 1 more hr at 0°. The reaction material was poured into ice water (500 ml) and the separated oil (a mixture of acyl azide and **17**) was taken up into toluene (100 ml). The dried, filtered toluene phase was then added dropwise to further toluene (10 ml) being heated on a steam bath with efficient stirring. In this way the vigorous nitrogen evolution was controllable. After gas evolution had ceased, removal of the solvent on a rotary evaporator left crude **1-norbornenyl isocyanate (17)**, pale yellow oil, λ^{neat} 4.47, 7.5 sharp (N=C=O), 14.05 (*cis* -CH=

CH–), containing a slight amount of toluene. The isocyanate could not be well separated from the toluene by distillation and, in fact, accompanied the toluene to some extent when the latter was removed on the rotary evaporator, as evidenced spectrally and by the intense lachrymatory and nasal-irritant qualities of **17**. The crude material was obtained in about 90% yield, however, and the reaction is probably nearly quantitative.

Treatment of the crude isocyanate (2 g) in ether with excess phenylmagnesium bromide for 2 hr at 25°, followed by hydrolysis with dilute sulfuric acid, threw down amide **18** as a crystalline solid. More **18** was obtainable from the ether phase. The combined material was decolorized in benzene with Norite and recrystallized several times from hot aqueous ethanol to afford pure amide **18** as white needles: yield, 1 g; mp 209.5–210° with sublimation from about 145°; λ^{KBr} 2.95, 3.08, 6.15, 6.56, 7.47, 7.63 (all –NHCO–), 6.35 weak (>C=C<), 14.18 (*cis* –CH=CH–), aromatic absorption evident at 6.7 and in the range 13.8–14.5; δ^{CDCl_3} 7.82 m, 7.45 m (ArH), 6.80 m (NH), 6.28 d (C-2 vinyl H, J_{AB} = 5.5 cps), 6.10 q (C-3 vinyl H, J_{BX} = 3 cps), 2.87 m (bridgehead H), 2.2–0.92 m (other ring H's).

Anal. Calcd for $C_{14}H_{15}ON$: C, 78.84; H, 7.09. Found: C, 79.07; H, 7.19.

When the isocyanate **17** was allowed to stand for 2 days in moist ether, large white crystals of **N,N'-di-(1-norbornenyl)urea** (**19**) formed. The solid was recrystallized from aqueous ethanol: mp 255–256° dec, sublimed from about 180°; λ^{KBr} 3.02, 6.12, 6.49, 7.47 (all –NHCO–), 14.15 (*cis* –CH=CH–).

Anal. Calcd for $C_{15}H_{20}ON_2$: N, 11.47. Found: N, 11.26.

exo-**3-Chloro-1-norbornylamine** (**21**).—The reaction of acid chloride **5a** and sodium azide in benzene described above was processed by adding excess concentrated hydrochloric acid and heating for 3 hr instead of adding ethanol, etc., as in the preparation of **14**. Separation of the acid layer and evaporation to dryness left a solid mass which was recrystallized several times from a mixture of isopropyl alcohol and ether using decolorizing carbon. The **amine hydrochloride 20** was obtained in this way as a white, microcrystalline solid: yield, 70%; mp 247–249° dec; λ^{KBr} 3.5 broad, 3.95, 5.2 broad, 6.3, 6.4 (all indicate $-NH_3^+$); δ^{CF_3COOH} 7.5 m (broad, $-NH_3^+$), 4.13 m (>CHCl), 2.7–1.4 m (other ring H's).

Anal. Calcd for $C_7H_{13}Cl_2N$: C, 46.18; H, 7.19; ionic Cl, 19.47. Found: C, 46.47; H, 7.22; ionic Cl, 19.29 (Volhard).[17]

The parent amine **21** was easily obtained from the salt by treatment with base and extraction with ether (white solid, reacts quickly with CO_2 in air, mp about 60°, δ^{CCl_4} 3.97 m (>CHCl), 2.4–1.2 m (other ring H's), 1.2 s ($-NH_2$). Conversion of **21** to the **phthalimide** derivative **22** and its purification were achieved as described for **15**. The derivative formed white spears: yield, 50%; mp 164–165°; λ^{KBr} 5.7, 5.9 (imide C=O); δ^{CCl_4} 7.8 m (ArH), 4.03 m (>CHCl), 3.4–1.2 m (other ring H's).

Anal. Calcd for $C_{15}H_{14}O_2ClN$: C, 65.33; H, 5.12. Found: C, 65.19; H, 5.40.

Neither the amine **21** nor the phthalimide **22** gave silver chloride when treated with alcoholic silver nitrate containing some nitric acid at 25°, though cloudiness developed slowly on warming. When the amine salt **20** (5.2 mmoles) was refluxed for 6 hr with 3 equiv of potassium *t*-butoxide in *t*-butyl alcohol (50 ml) and then poured into water, ether extraction afforded only amine **21** (essentially total recovery). No product with the strong 14 μ infrared absorption characteristic of the norbornenes was detected.

1-Norbornenyl Acetate (**23**).—*exo*-2-Bromonorbornane-1-carboxylic acid chloride[14a] (19.25 g, 0.08 mole) was refluxed in dry toluene containing 0.1 mole of activated sodium azide for 43 hr protected from atmospheric moisture. The cooled solution was filtered from the precipitated sodium chloride, which was washed well with further toluene. Hydrochloric acid (concentrated, 80 ml) was then added to the toluene solution and the mixture was heated under reflux with vigorous stirring for 2 hr. Separation of the acid phase and its evaporation to dryness under vacuum left a solid mass which was taken up into methanol and filtered. The volume of the filtrate was reduced and carbon tetrachloride then added to precipitate *exo*-**2-bromo-1-norbornylamine hydrochloride** (**24**) as a white, microcrystalline solid: yield, 15.7 g (85%); mp 161–163° from methanol–ethyl acetate, solvate with carbon tetrachloride mp 165–168°; λ^{Nujol} 3.2–4.0, 5.0, 6.3, 6.67 ($-NH_3^+$); δ^{D_2O} 4.37 m (>CHBr), 2.5–1.3 m (all other ring H's).

Anal. Calcd for $C_7H_{13}BrClN$: C, 37.11; H, 5.78. Found: C, 37.20; H, 5.82.

Derivatization *via* acylation of this highly reactive amine proved difficult because of the rapid formation of norcamphor in most cases. But the benzamide was finally obtained as follows. A dispersion of the salt **24** (1 g) in benzene (10 ml) and benzoyl chloride (4 ml) was treated with pyridine (5 ml) dropwise. The mixture was then warmed at 60° for 30 min and poured into water. The benzene layer was separated, washed with 5% sodium carbonate solution, dried, and evaporated. The residue was purified from hot cyclohexane, followed by recrystallization several times from benzene–petroleum ether (bp 30–60°) mixtures to give **N-(*exo*-2-bromo-1-norbornyl)benzamide** as white fluffy needles: yield, 60–85%; mp 147–148°; $\lambda^{Fluorolube}$ 3.08, 6.1, 6.5; λ^{Nujol} 7.56 (all amide bands); δ^{CDCl_3} 7.79 m, 7.41 m (ArH), 6.73 broad (–CONH–), 4.68 m (>CHBr), 2.5–1.2 m (other ring H's).

Anal. Calcd for $C_{14}H_{16}OBrN$: C, 57.15; H, 5.48; N, 4.76. Found: C, 57.56; H, 5.53; N, 4.68.

The amine salt **24** (2.0 g, 8.8 mmoles) was diazotized in acetic acid (30 ml) containing acetic anhydride (2 ml) at 25° by the addition of solid sodium nitrite (2 g) in portions with stirring. The mixture was stirred after the addition for 1 hr and the process repeated (2 g further of sodium nitrite). The mixture was neutralized with solid sodium carbonate (in a large beaker) and extracted thoroughly with pentane. The extracts were washed well with water to neutrality, dried, and evaporated. The residue was distilled in a short-path apparatus to afford *exo*-**2-bromo-1-norbornyl acetate** (**25**) as a pale yellow oil: yield, 1.48 g (72%); bp 122–127° (20 mm); $n^{4.5}D$ 1.5112; λ^{neat} 5.77 (C=O), 7.98, 8.19 (acetate C—O); δ^{CCl_4} 4.78 m (>CHBr), 2.1 s ($-OCOCH_3$), 2.5–1.3 m (other ring H's). The analytical sample was obtained as a colorless, pleasant-smelling oil by short-path distillation in a Hickman still.

Anal. Calcd for $C_9H_{13}O_2Br$: C, 46.36; H, 5.61. Found: C, 46.24; H, 5.64.

A mixture of ester **25** (500 mg, 2.1 mmoles) was heated at 180–200° in a sealed tube with *sym*-collidine (4.75 g) and 3,5-lutidine[23] (0.25 g) for 7 days, though there is reason to believe this long time was not necessary. The cooled tube was opened, filtered from the amine salts, and poured into excess concentrated hydrochloric acid and ice. The acidic solution was extracted well with methylene chloride. Removal of the solvent left a brown oil which was codistilled with water to afford **23** as a colorless oil (110 mg, 34%) after decantation and drying. The neat infrared spectrum showed absorptions at 3.3 (=CH), 6.40 weak (>C=C<), 14.05 (*cis* –CH=CH–), 5.73 (C=O), 7.96, 8.15 (acetate C–O), identical in detail with that found by Norton.[10]

1-Norbornenyl Chloride (**27**).—2,2-Dichloronorbornane[18] (**28**, 330 g, 2 moles) in carbon tetrachloride (1 l.) was treated with anhydrous aluminum chloride (1–2 g) and allowed to stand with occasional stirring for 3 days. The mixture was filtered from some tarry material and the nearly colorless filtrate was then vacuum distilled at a pressure such that the head temperature remained at about 35° to remove the solvent. Glpc analysis then followed (silicone rubber, SE-30, 110°). The treatment with aluminum chloride and carbon tetrachloride as described was repeated several times until an analysis indicated about a 4:1 mixture of 1,2-dichloride–2,2-dichloride was obtained: yield, 225 g; bp 93–100° (24 mm). This was then fractionated carefully through a 45-cm Vigreux column (1 drop/10 sec) to obtain a mixture enriched in *vic*-dichloride: bp 57–58° (2.7 mm); yield, 112 g (*ca.* 90% pure). Repeated distillations eventually gave glpc-pure **1**, *exo*-**2-dichloronorbornane** (**29**), and a colorless oil: bp 77° (11 mm); $n^{25}D$ 1.5019, mp 6–7°; yield, 25 g; δ^{CCl_4} 3.94 m (>CHCl), 2.5–1.55 m (other ring H's).

Anal. Calcd for $C_7H_{10}Cl_2$: C, 50.93; H, 6.11. Found: C, 51.30; H, 6.22.

More halide could be obtained by recycling the distillation residues through the isomerization process and isolation again as above. Although little loss occurred in these operations, some norcamphor (**26**) was formed and 1-*endo*-2-dichloronorbornane (**30**, see later) began to accumulate in the product as well. The former was easily removed by washing with water; the latter presented no problem in the following reaction in that it was inert.

A sample of the *vic*-dichloride **29** that contained some *endo* epimer **30** (60.8 g, 0.37 mole) was added slowly to hot (120°) potassium hydroxide (42 g of 85% material; 0.64 mole) in

triethylene glycol (200 ml). The temperature was raised to 135–140° and water codistilled with the dehydrochlorinated product into a water separator. The oily layer was separated from the distillate and the water returned to the reaction vessel. The oil was dried and distilled to give pure 1-norbornenyl chloride (**27**), bp 80–95° (95 mm), and a higher boiling fraction, bp 137° (95 mm). This latter material was treated again with base as described to give more **27** and a higher boiling fraction that now proved resistant to further dehydrochlorination. Pure **27** was obtained as a colorless oil: yield, 27 g (68.5%); bp 139.5–141° (750 mm), 75.5–77.5° (95 mm); $n^{25}D$ 1.4817; d_4^{25} 1.043; MD calcd 34.53, found 34.51; λ^{neat} 3.3 (=CH), 6.4 (>C=C<), 14.08 (*cis* -CH=CH-); δ^{CCl_4} 6.02, 5.89 m (-CH=CH-, J_{AB} = 5.6 cps, J_{AX} = 3.5 cps, $J_{BX} \sim$ 1 cps), 2.81 m (bridgehead H), 2.0–1.0 m (other ring H's). The chloride showed one peak on several glpc columns.

Anal. Calcd for C_7H_9Cl: C, 65.37; H, 7.06; Cl, 27.57. Found: C, 65.38; H, 6.98; Cl, 27.45.

The higher boiling fraction, **1-*endo*-2-dichloronorbornane** (**30**), eventually solidified: yield, 9.48 g (15.6% of initial dichloride); mp 31–32.5° after sublimation; bp 135–137° (90–95 mm); δ^{CCl_4} 4.32 m (>CHCl), 2.24 m (bridgehead and *exo* C-3 H's), 2.1–1.1 m (other ring H's). This dichloride, upon treatment with aluminum chloride in carbon tetrachloride for 2 days at 25°, isomerized to the *gem*-dichloride **28** (20%) and a mixture of 1,2-dichlorides (80%, *ca.* four parts *exo* to one part *endo*), as shown by glpc (SE-30, 110°). This mixture was the same as that obtained from **28** (see earlier) and probably represents the equilibrium composition of the three dichloride under these conditions.

Study of the Reactivity of 1-Norbornenyl Chloride (27). Attempted Solvolyses.—(1) A mixture of chloride **27** (250 mg), purified dioxane (2.5 ml), and water (2.5 ml) saturated with silver nitrate was heated in a sealed tube at 160° for 113 hr. The tube was cooled and a voluminous precipitate of a gray solid was noticed. *The tube exploded violently* upon being opened. What precipitate was recovered proved to be nearly pure silver. (2) Chloride **27** (5 g) was refluxed in 80% ethanol saturated with silver nitrate in the dark for 370 hr. Collection and examination of the small amount of precipitate formed in this time indicated it to be mainly silver, but the presence of 2.6% silver chloride could be established. (3) Chloride **27** (250 mg) was mixed with purified dioxane (2 ml) and saturated lead acetate solution (1 ml). The initially nonhomogeneous solution coalesced as it was heated to 150° for 7 days in a sealed tube. Examination of the contents after this time revealed no change in the components whatsoever.

Chloride **27** proved adamant to reaction with lithium or magnesium under several sets of conditions. Utmost care was taken to provide favorable conditions but **27** was always recovered unchanged.

Treatment of **27** with phenyl azide precisely as described for its reaction with norbornene[52] led to a very low yield of an adduct, assigned the structure **32**. Except for its infrared spectrum, which was very similar to that of the norbornene–phenyl azide adduct, no other characterization of **32** was attempted. That conditions were proper for reaction was established by the preparation of the norbornene adduct with phenyl azide, 60%, mp 97.5–98.5° (lit.[52] mp 101°).

A mixture of chloride **27** (1.13 g, 8.8 mmoles) and 1,2,3,4-tetrachloro-5,5-dimethoxycyclopentadiene[53] (2.3 g, 8.8 mmoles) was heated in a pressure bottle at 105° for 3.5 days. The oily product was taken up in ethanol, decolorized, and filtered. Addition of water to turbidity followed by chilling gave the adduct, **33**: yield, 2.42 g (71%); mp 93–93.5° after several recrystallizations from methanol; λ^{Nujol} 6.26 (>C=C<), 8.41 (>C–O); δ^{CCl_4} 3.58 s, 3.52 s (two $-OCH_3$), 2.67 t (ring junction H's, an AB pattern with overlap of center lines, J_{AB} = 9 cps), 2.52 m (bridgehead H), 2.0–1.2 m (other ring H's).

Anal. Calcd for $C_{14}H_{15}O_2Cl_5$: C, 42.84; H, 3.85. Found: C, 42.70; H, 3.89.

The infrared spectrum of **33** was very similar to that of the norbornene adduct, prepared in a similar manner, mp 104–105° (lit.[54] mp 106–107°).

(52) P. Shcheiner, J. H. Schomaker, S. Deming, W. J. Libbey, and G. P. Nowak, *J. Am. Chem. Soc.*, **87**, 306 (1965).

(53) J. S. Newcomer and E. T. McBee, *ibid.*, **71**, 946 (1949).

(54) K. Mackenzie, *J. Chem. Soc.*, 473 (1960).

Chloride **27** was hydrogenated in ethanol containing potassium hydroxide (Pd/C, 2 atm) to afford 1-norbornyl chloride (**31**), mp 37–39° (lit.[18a] liquefies by 43°), identical with an authentic sample.

Upon storage in a corked vessel in a refrigerator for 2 weeks, chloride **27** developed color and the presence of hydrogen chloride was obvious. The material showed λ^{neat} 3.7 and 5.8 μ, indicating aldehydic contamination which was proved also by a positive 2,4-DNP test. The chloride could be stored unchanged in sealed vessels under nitrogen.

Thermal Behavior of Chlorides.—2,2-Dichloronorbornane (**28**) lost hydrogen chloride when heated under reflux at atmospheric pressure. Subsequent distillation afforded nearly pure **2-norbornenyl chloride**: bp 140–150° (752 mm), λ^{neat} 6.3 (>C=C<), no absorption at 14; δ^{CCl_4} 5.75 d (=CHCl, J_{AX} = 4 cps, though higher order splitting was also apparent), 2.88 m (two bridgehead H's), 2.0–1.0 m (other ring H's). The chloride was identical with that produced from **28** by either a literature method[55] or by use of potassium hydroxide in triethylene glycol just as described above for **27**. 2-Norbornenyl chloride itself decomposed on SE-30 glpc columns over 190° to two more volatile substances, possibly ethylene and chlorocyclopentadiene. But such decompositions carried out in boiling tetralin in the presence of maleic anhydride failed to produce an adduct of the chlorodiene and the exit gases failed to decolorize bromine solutions. So the nature of the cleavage products remains obscure. Exactly analogous behavior to the above was observed with 1-*exo*-2-dichloronorbornane (**29**) and with 1-norbornenyl chloride (**27**), except that each of these required about 30° higher temperatures for dissociation.

Phenyl 1-Norbornenyl Ketone (**34**).—Diphenylcadmium was prepared by reaction of phenyl Grignard reagent (3 *M*, 33 ml) with cadmium chloride (anhydrous, 0.97 g) in ether. The ether was replaced by benzene (60 ml) and stirred until a fine suspension was obtained. Acid chloride **5a** (5.2 g, 33 mmoles) in benzene (20 ml) was then added and the solution was refluxed for 1 hr. After acidification, the benzene phase was separated and washed with sodium carbonate solution and brine. Removal of the benzene left crude **34** which was purified by the addition of Girard-T reagent (6.4 g) in acetic acid (7 ml). The mixture was refluxed for 1 hr, cooled, and neutralized with base. Water was added to increase the volume to *ca.* 250 ml and nonketonic by-products were then removed by thorough extraction with ether. The aqueous phase was then strongly acidified with hydrochloric acid and allowed to stand 1 hr. Extraction of the liberated oil with ether and preparative glpc (SE-30, 175°) then afforded the ketone **34** as a pale yellow oil: yield, 0.63 g (9.75%); λ^{neat} 5.95 (Ar–C=O); δ^{CCl_4} 8.05 m, 7.5 m (ArH), 6.31 m (-CH=CH-), 3.07 m (bridgehead H), 2.5–1.0 m (other ring H's).

Anal. Calcd for $C_{14}H_{14}O$: C, 84.81; H, 7.12. Found: C, 84.49; H, 7.09.

The **2,4-dinitrophenylhydrazone** was prepared as an orange crystalline solid, mp 146–148° from ethanol.

Anal. Calcd for $C_{20}H_{18}O_4N_4$: N, 14.82. Found: N, 14.53.

Norbornene-1-carboxaldehyde (**35**).—This preparation followed closely the literature method *via* the N-acylaziridine.[29] It is crucial that all reactions be done below 5° in order to prevent formation of an oxazoline. From acid chloride **5a** (6.41 g, 0.04 mole) there was obtained the colorless, pleasant-smelling aldehyde **35**: yield, 2.66 g (53%); bp 44° (6.4 mm); $n^{25}D$ 1.4829; d_{27}^{27} 1.001; λ^{neat} 3.5, 3.61, 5.75 (-CH=O), 6.32 (>C=C<), and 14.0 (*cis* -CH=CH-); δ^{CCl_4} 10.1 s (CHO), 6.27 m, 6.10 m (-CH=CH-), 3.1 m (bridgehead H), 2.2–1.0 m (other ring H's).

Anal. Calcd for $C_8H_{10}O$: C, 78.65; H, 8.25. Found: C, 78.42; H, 8.36.

The **2,4-dinitrophenylhydrazone** was yellow-orange, mp 176–178° from ethanol–ethyl acetate.

Anal. Calcd for $C_{14}H_{14}O_4N_4$: N, 18.51. Found: N, 18.31.

The **tosylhydrazone** derivative **36**, prepared as described[30] for the saturated analog, was a white, microcrystalline solid, mp 137–139° dec from aqueous ethanol.

Anal. Calcd for $C_{15}H_{18}O_2N_2S$: C, 62.04; H, 6.25. Found: C, 62.03; H, 6.25.

Norbornenyl-1-carbinol (**37**).—Reduction of the methyl ester **9** (4 g, 20.6 mmoles) with lithium aluminum hydride in ether in the standard fashion gave the alcohol **37** as a colorless oil:

(55) N. A. LeBel, *J. Am. Chem. Soc.*, **82**, 623 (1960).

yield, 2.7 g (94.5%); bp 46–48° (0.15 mm); λ^{neat} 2.96 (OH), 6.36 weak (>C=C<), 9.8 (CH_2–OH), 14.1 (*cis* –CH=CH–); δ^{CDCl_3} 6.12 q (C-3 vinyl H, J_{AB} = 5.9 cps, J_{AX} = 3 cps), 5.95 d (C-2 vinyl H), 3.92 s (CH_2OH), 2.85 m (bridgehead H), 1.9 s (OH), 2.0–0.95 m (other ring H's).

Anal. Calcd for $C_8H_{12}O$: C, 77.40; H, 9.74. Found: C, 77.23; H, 9.84.

Hydrogenation of **37** (95% ethanol, Pd/C, 3 atm) gave **norbornyl-1-carbinol** (**39**), 88.5%, mp 48–52° (lit.[18] mp 58–63, 59–60.2°), identical spectrally with authentic material.

Norbornenyl-1-carbinyl tosylate (**38**) was prepared from the alcohol and tosyl chloride in pyridine in the usual fashion: yield, 82%; mp 84.5–86° from benzene–petroleum ether (bp 30–60°); λ^{CS_2} 7.3, 8.45 (–OSO_2–), 14.1 (*cis* –CH=CH–); δ^{CDCl_3} 7.90 d, 7.42 d (ArH, J = 8.5 cps), 6.12 q (ABX, C-3 vinyl H, J_{AB} = 6 cps, J_{AX} = 3 cps), 5.85 d (C-2 vinyl H), 4.35 s (–CH_2–O–), 2.87 m (bridgehead H), 2.47 s (Ar–CH_3), 2.0–0.90 m (other ring H's).

Anal. Calcd for $C_{15}H_{18}O_3S$: C, 64.72; H, 6.50. Found: C, 64.92; H, 6.67.

The saturated analog, **norbornyl-1-carbinyl tosylate** (**42**), was prepared as reported: yield, 82.5%; mp 76–78° (lit.[18b] mp 78.9–80°).

Norbornenyl-1-acetic Acid (**40**).—Acid chloride **5a** (7.0 g, 0.045 mole) was converted into the diazoketone by treatment with excess diazomethane in ether. After 12 hr the ether and excess diazomethane were removed by water aspiration. The oily residue, λ^{neat} 4.72 (–$COCHN_2$), was dissolved in aqueous tetrahydrofuran (50% v/v, 150 ml) and irradiated with a low-pressure ultraviolet lamp for 57 hr, during which time 70% of the expected nitrogen was liberated. The solution was made basic with sodium bicarbonate solution and washed several times with ether. The boiled alkaline phase was then acidified and reextracted with several portions of ether. The dried extracts were combined and distilled to give acid **40** as a colorless oil that solidified on standing: yield, 1.14 g (16.5%); bp 98–99° (1.7 mm); mp 38.5–40° after sublimation; λ^{KBr} 3.1–3.9, 5.80 (COOH), 6.31 weak (>C=C<), 14.1 (*cis* –CH=CH–); δ^{CCl_4} 12.15 s (COOH), 6.05 m (–CH=CH–), 2.9 m (bridgehead H), 2.75 s (–CH_2–COOH), 2.0–0.9 m (other ring H's).

Anal. Calcd for $C_9H_{12}O_2$: C, 71.03; H, 7.95; neut equiv, 152.2. Found: C, 71.03; H, 8.05; neut equiv, 152.8.

The **S-benzylisothiuronium salt** was prepared and recrystallized once from dioxane and several times from 95% ethanol, mp 155–156.5°.

Anal. Calcd for $C_{17}H_{22}O_2N_2S$: C, 64.12; H, 6.96; N, 8.80. Found: C, 64.50; H, 7.12; N, 8.83.

Acid **40** could be converted by hydrogenation into **norbornyl-1-acetic acid** (**41**): bp 108–110° (1.25 mm); neut equiv, calcd 154.2, found 152.5; λ^{neat} 3.2–4.0, 5.85 (COOH), no unsaturation evident at *ca.* 6.2 or 14; δ^{CCl_4} 11.7 s (COOH), 2.53 s (–CH_2–COOH), 2.23 m (bridgehead H), 1.9–1.2 m (other ring H's). The saturated acid formed an **S-benzylisothiuronium salt,** mp 163.5–165° from dioxane.

Anal. Calcd for $C_{17}H_{24}O_2N_2S$: N, 8.74. Found: N, 8.93.

As an independent synthesis of **41**, its methyl ester (82%, bp 56–58° (0.75 mm), λ^{neat} 5.77 (C=O), 9.0 (C–O–C)) was prepared from acid **11** by an Arndt–Eistert sequence.[56] Saponification of the ester gave the saturated acid (87%) identical with the sample prepared from acid **40** by hydrogenation.

Solvolysis (Hydrolysis) Study.—Separate solutions of tosylate **38** and tosylate **42**, each 0.03 *M* in tosylate and in 60% reagent grade acetone–40% distilled water (v/v) containing *sym*-collidine (freshly distilled Matheson material but not otherwise purified, 0.033 *M;* the material was probably a mixture[57]), were prepared in ampoules, sealed, and held at various constant temperatures (see Table I). Ampoules were removed at time *t*, cooled quickly, opened, and rinsed into a titration flask with additional acetone (10 ml). Water (10 ml) was next added and the remaining collidine was then measured by titration with hydrochloric acid (0.0146 *M*) to a bromphenol blue end point (blue to turquoise), using a standardization curve determined by titration of collidine alone under the same conditions. The rate constants were determined graphically from the slope of the line $\ln T_0/T_t$ *vs.* time, where T_0 is the initial titer and T_t is the titer at time *t*. The reactions were followed to 50–85% completion and showed little drift in rate. The parameters ΔH^* and ΔS^* were calculated from the Eyring equation.

The procedure for product isolation and characterization was similar to the kinetic procedure, except it was some fivefold larger in scale. Mixtures of the appropriate tosylate, solvent, and *sym*-collidine were again made 0.03 *M* in the tosylate and 0.033 *M* in the collidine. The solution (125 ml) was placed into a pressure bottle and incubated in an oven at 113° for 48 hr. After this time the solution was saturated with salt and thoroughly extracted with several portions of ether. Isolation of the products was by glpc (neopentyl glycol disuccinate, 180°).

From tosylate **42** was obtained an inseparable mixture of **norbornyl-1-carbinol** (**39**) and **1-bicyclo[2.2.2]octanol** (**43**), 8.5%:91.5%, respectively, about 90% yield, mp 197–201° (s.t.). The composition was established by comparison with a synthetic mixture available from other work[30] using glpc, infrared, and nmr data. Alcohol **39** was conspicuous in the nmr spectrum by virtue of the δ 3.75 s (–CH_2OH) resonance. From tosylate **38** was similarly obtained a mixture of **norbornenyl-1-carbinol** (**37**) and **bicyclo[3.2.1]oct-6-en-1-ol** (**44**), 42%:58%, respectively, in about 90% yield. The alcohols were separable by glpc and **37** was identified by comparison with authentic material. The octenol **44** was a white crystalline solid with a pleasant odor: mp 158.5–160.5° (s.t.); λ^{CS_2} 2.79, 3.0 (OH), 8.8, 9.03 (tertiary C–O), 13.6 (*cis*–CH=CH–), δ^{CDCl_3} 5.76 m (–CH=CH–), 2.71 m (bridgehead H), 1.87 s (OH, removed by D_2O), 2.2–1.2 m (other ring H's).

Anal. Calcd for $C_8H_{12}O$: C, 77.40; H, 9.72. Found: C, 77.26; H, 9.64.

When the collidine was omitted, only **43** (again in high yield) was isolable from **42**. Likewise, only **44** resulted from **38** under these conditions, but its yield was reduced (~50%).

Control experiments were performed wherein the individual product alcohols were heated at 113° in the hydrolysis solvent containing an equivalent of *p*-toluenesulfonic acid but no collidine. The alcohols were then isolated as before and examined spectrally for the changes in composition noted in Table II. All the hydrolysis products were thus shown to be stable to the acidic medium generated in the absence of collidine except **37**. This alcohol was sensitive to acid[58] and was changed to a complex mixture lacking the 14.1-μ infrared absorption characteristic of the unsubstituted norbornene double bond and giving a positive 2,4-DNP test. So collidine was necessary to detect **37** in the hydrolysate. In addition, aldol condensation products from the acetone were absent when collidine was employed. These caused serious drift in rate in its absence.

Neither acetolysis nor formolysis of **38** was investigated in detail. The acetolysis rate decreased markedly after about 33% completion, indicating probable ion-pair return.[59] Also, the solutions colored badly and titration end points were difficult to see. Cursory spectral examination of the solvolysate indicated some addition to the double bond had also occurred. The acetolysis of **42**, on the other hand, was performed as reported (k_1 = 11.32 × 10^{-6} sec^{-1} at 99.5° (lit.[18b] k_1 = 11.69 × 10^{-6} sec^{-1} at 99.7°) with no difficulty. The reaction product was **1-bicyclo[2.2.2]octyl acetate** (λ^{neat} 5.76 (C=O), 8.0 (acetate C—O)), confirmed by comparison with a known sample. A brief examination of formolysis showed that **42** could be studied, but not **38**. Solutions of the latter became badly colored and spectral examination again indicated that addition of solvent to the double bond was occurring.[60]

Decomposition of tosylhydrazone 36 in N-methylpyrrolidone was carried out in the general manner described earlier.[30] Several decompositions were studied (1–2 g of **36**) and the alcohol products isolated by glpc (Carbowax 20M, 180°). The product mixture, which could not be resolved, was a fragrant white solid: yield, *ca.* 10%; mp 89–105°; δ^{CCl_4} 6.10 m, 5.70 m (two separate –CH=CH–), 3.80 s (–CH_2OH), 3.55 s (broad, concentration dependent, OH), 2.70 m, 2.42 m (two bridgehead H's, but not in equal percentages), 2.2–1.0 m (other ring H's). The infrared spectrum showed the alcohols to be mainly tertiary (λ^{KBr} *ca.* 9 μ) and integration of the nmr spectrum showed the

(56) M. S. Newman and P. F. Beal, III, *J. Am. Chem. Soc.*, **72**, 5163 (1950).

(57) *Cf.* Brown, Johnson, and Podall[43] for a discussion of the purity of commercial *sym*-collidine.

(58) We thank Mr. P. Chenier for this investigation.

(59) R. S. Bly and co-workers[8] found deviation in acetolysis rates after 30–40% completion in their study of the brosylate of **37**. Ion-pair return to the brosylate of **45** occurred (18%).

(60) Witness the addition of formic acid to norbornene by D. C. Kleinfelter and P. von R. Schleyer, *Org. Syn.*, **42**, 79 (1962).

composition to be **37**, 9%, **44**, 47%, and another alcohol, 44%. The infrared spectrum of the mixture showed a certain resemblance to that of 1-bicyclo[2.2.2]octenol (**45**)[61] and the resonance at δ 2.42 in the nmr spectrum was clearly that of a bridgehead proton of another alcohol similar in structure to **44**. On these considerations, the other major product was assigned structure **45**. Other products isolated in variable yield from **36** were *p*-tolyl disulfide and *p*-tolyl *p*-toluenethiolsulfonate, characterized as before.[30]

Registry No.—**5**, 15023-39-9; **5**, S-benzylisothiuronium salt, 15023-57-1; **5**, phenacyl ester, 15026-12-7; **5a**, 15023-40-2; **7**, 698-39-5; **7**, S-benzylisothiuronium salt, 15023-42-4; ethyl ester of **7**, 15023-43-5; methyl norbornene-2-carboxylate, 701-15-5; **8**, 15023-45-7; **9**, 15023-46-8; **10**, 15023-47-9; **12**, 15023-48-0; **13**, 15023-49-1; **14**, 15023-50-4; **15**, 15023-51-5; **18**, 15023-52-6; **19**, 15023-53-7; **20**, 25023-54-8; **21**, 15023-55-9; **22**, 15023-56-0; **23**, 15019-68-8; **24**, 15019-69-9; **25**, 15019-70-2; **27**, 15019-71-3; **29**, 15019-72-4; **30**, 15019-73-5; **33**, 15019-74-6; **34**, 15019-75-7; **34**, 2,4-dinitrophenylhydrazone, 15019-76-8; **35**, 15019-77-9; **35**, 2,4-dinitrophenylhydrazone, 15019-78-0; **36**, 15019-79-1; **37**, 6814-81-9; **38**, 15019-81-5; **40**, 15019-82-6; **40**, S-benzylisothiuronium salt, 15156-48-6; **41**, 15019-83-7; **41**, S-benzylthiuronium salt, 15156-49-7; **41**, methyl ester, 15019-84-8; **44**, 15019-85-9; N-(*exo*-2-bromo-1-norbornyl)benzamide, 15019-86-0; ethyl norbornene-1-carboxylate, 15019-87-1; 2-norbornenyl chloride, 694-93-9.

(61) A. B. Sayigh, Dissertation, Columbia University, 1954.

Acknowledgment.—This work was supported by the Army Research Office (Durham), Contract DA-31-124-ARO(D)-69, to whom we express our appreciation. We thank Professor R. S. Bly and his associates at the University of South Carolina for much information on their related studies in advance of publication and for their assistance in determining some of the nmr spectra.

Synthesis of Deoxyguanylyldeoxyguanosine on an Insoluble Polymer Support[1,2]

TAKEO SHIMIDZU[3] AND R. L. LETSINGER

Department of Chemistry, Northwestern University, Evanston, Illinois 60201

Received July 26, 1967

Procedures are described for attaching N-dimethoxytrityldeoxyguanosine to an insoluble polymer support and for converting the resulting derivative into N-dimethoxytrityldeoxyguanylyl(N-dimethoxytrityl)deoxyguanosine and deoxyguanylyldeoxyguanosine.

In the synthesis of oligonucleotides on polymer supports 5′-O-trityldeoxycytidine and thymidine have been utilized as anchor nucleosides. Trityldeoxycytidine was joined to the support through the amino group of the cytosine ring;[4] thymidine was joined at the 3′-O[5] and 5′-O[6] of the deoxyribose ring. The nucleotide chain has been lengthened both by the phosphodiester route[5,6] developed by Khorana for reactions in solution and by the phosphotriester route.[4] In extending the scope of the syntheses on insoluble polymer supports we have investigated the possibility of utilizing deoxyguanosine as an anchor nucleoside and of building the chain by addition of deoxyguanosine units by the phosphotriester approach. The present paper reports the synthesis of deoxyguanylyldeoxyguanosine by this method. Deoxyguanylyldeoxyguanosine was previously prepared by Schaller and Khorana with a homogeneous reaction system.[7]

The support was an insoluble polymer made from styrene (89 mole %), *p*-divinylbenzene (0.1%), and *p*-vinylbenzoic acid (11%). It was converted to the acid chloride (Ⓟ—COCl),[8] I, by reaction with thionyl chloride in benzene[9] and then treated with excess N-di-*p*-methoxytrityldeoxyguanosine[10] in pyridine for a period of 48 hr. Residual acid chloride groups were esterified by reaction with methanol (Chart I) and the polymer II was collected, washed, dried, and weighed. As judged by the increase in weight (I → II), polymer II contained 0.46 mmole of N-dimethoxytrityldeoxyguanosine per gram, which corresponds to esterification of 61% of the carboxyl groups in the initial support with N-dimethoxytrityldeoxyguanosine.

Polymer II was phosphorylated with β-cyanoethyl phosphate with dicyclohexylcarbodiimide as the activating agent. The extent of phosphorylation was estimated by hydrolyzing a portion of the product with alkali and eluting the nucleotidic material; after removal of the dimethoxytrityl groups by acid hydrolysis, the deoxyguanosine and deoxyguanosine phosphate were separated by paper chromatography and assayed spectrophotometrically. These experiments showed that 58% of the dimethoxytrityldeoxyguanosine on the support was phosphorylated within 9 days. It is noteworthy that the solvent (solvent C) used in the paper chromatography serves to separate deoxyguanosine 3′-phosphate from deoxyguanosine-5′

(1) Part IX in series on Nucleotide Chemistry. For part VIII see R. L. Letsinger and K. K. Ogilvie, *J. Am. Chem. Soc.*, **89**, 4801 (1967).

(2) This research was supported by the Division of General Medical Sciences, National Institutes of Health, GM-10265.

(3) Department of Hydrocarbon Chemistry, Kyoto University, Kyoto, Japan.

(4) R. L. Letsinger and V. Mahadevan, *J. Am. Chem. Soc.*, **87**, 3526 (1965); **88**, 5319 (1966).

(5) R. L. Letsinger, D. M. Jerina, and M. H. Caruthers, *Biochemistry*, **6**, 1397 (1967).

(6) H. Hayatsu and H. G. Khorana, *J. Am. Chem. Soc.*, **88**, 3182 (1966); F. Cramer, R. Helbig, H. Hettler, K. H. Scheit, and H. Seliger, *Angew. Chem.*, **78**, 640 (1966); L. R. Melby and D. R. Strobach, *J. Am. Chem. Soc.*, **89**, 450 (1967).

(7) H. Schaller and H. G. Khorana, *ibid.*, **85**, 3828 (1963).

(8) Ⓟ refers to the portion of the insoluble polymer other than the active functional groups.

(9) R. L. Letsinger, M. J. Kornet, V. Mahadevan, and D. M. Jerina, *ibid.*, **86**, 5163 (1964).

(10) The dimethoxytrityl group is used to protect the guanine ring in the subsequent phosphorylation steps. It was introduced for this purpose by H. Schaller, G. Weimann, B. Lerch, and H. G. Khorana, *ibid.*, **85**, 3821 (1963).