Solvolysis of Optically Active 1,2-Dimethyl-5-norbornen-*exo*-2-yl *p*-Nitrobenzoate. Direct Evidence for a Classical Carbonium Ion

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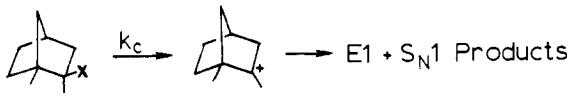
Abstract: Solvolysis of optically active 1,2-dimethyl-5-norbornen-*exo*-2-yl *p*-nitrobenzoate (**11**) in 90% acetone gives 2-methylene-1-methyl-5-norbornene (**15**) (62% retention of configuration), 1,2-dimethyl-5-norbornen-*exo*-2-ol (**14**-OH) (15% retention), and racemic 1,6-dimethyl-3-nortricyclanol (**16**-OH). Results for methanolysis are similar: the E1 and S_N1 products (**15** and **14**-OMe) are formed with 60 and 14% retention of configuration and the 1,6-dimethyl-3-nortricyclyl methyl ether (**16**-OMe) is racemic. Acetolysis of optically active 5-norbornen-*exo*-2-yl *p*-bromobenzenesulfonate (**6**) gives racemic products. These results indicate that change from the parent secondary norbornenyl system (**6**) to the tertiary system (**11**) results in change from assisted ionization to form the symmetrical norbornenyl-nortricyclyl cation (**7**) to unassisted ionization to give the asymmetric tertiary classical cation (**12**) which subsequently is converted to the symmetrical 1,2-dimethyl-3-nortricyclyl cation (**13**).

In earlier studies we investigated tertiary *exo*-2-norbornyl (**1**)[1] and *exo*-2-benzonorbornenyl systems (**2a**).[2] Our approach



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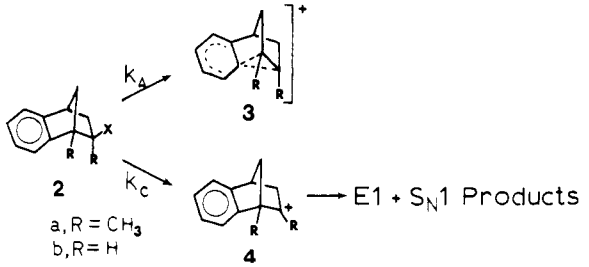
has been to use the 1,2-dimethyl derivatives so that the symmetry properties of product-forming intermediates can be used as a criterion for the nature of ionization, i.e., assisted to give a symmetrical bridged ion (e.g., **3**) or unassisted to give an unsymmetrical classical ion (**4**). The C-1 methyl substituent



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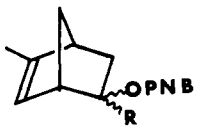
has only a minor accelerating effect in the tertiary norbornyl (~4)[3,4] and benzonorbornenyl systems (~5),[5] and from this we conclude that this substituent has no important effect on the ionization step.

Solvolysis of 1,2-dimethyl-*exo*-2-norbornyl (**1**)[1] and 1,2-dimethyl-*exo*-2-benzonorbornenyl derivatives (**2a**)[2] involves unsymmetrical classical intermediates. In each case, optically active chloride and *p*-nitrobenzoate gives active E1 (60–78% retention of configuration) and S_N1 (8–14% retention) products. From this we conclude that ionization changes from assisted (k_Δ) in the parent secondary systems (e.g., **2b**) to unassisted (k_c) in the tertiary systems (**1** and **2a**). This change results from the much larger accelerating effect of the α-methyl substituent on k_c (10^7–10^8) than on k_Δ.[6] The magnitude of an α-methyl substituent on k_Δ can be estimated for a related system. In the 5-methyl-5-norbornen-2-yl system (**5**) the exo/endo rate ratio drops from ~2×10^7 for **5b** to ~10^5 for **5a**. This indicates that the α-methyl substituent in **5a** increases unassisted ionization (endo isomers) about 200 times more than π assisted ionization (exo isomers). Thus it is clear that an α-methyl substituent has a much larger effect on k_c than on k_Δ.



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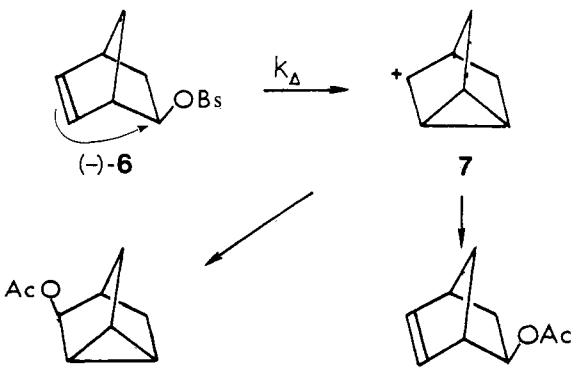
a, R = CH_3
b, R = H

We now report results of a similar investigation of the 5-norbornen-*exo*-2-yl system. In the parent secondary system π participation is clearly involved in acetolysis of the *p*-bromobenzenesulfonate (**6**). This is indicated by both kinetic[9] and product studies.[10] The exo/endo rate ratio for acetolysis of the *p*-bromobenzenesulfonates is higher than that for the norbornyl system.[9] Or to put it another way, the rate retarding inductive effect of the double bond is much larger for the endo isomer (>40-fold) than for the exo isomer (<2-fold) because in the latter π participation nearly cancels the retarding effect of the double bond.[11]

Cristol and co-workers[10b] have shown that acetolysis of *exo*-3-deuterio-**6** gives 5-norbornen-*exo*-2-yl acetate (**9**) that is equally labeled at the 3 and syn-7 positions. This indicates that the product-forming intermediate is symmetrical. In this connection it is noteworthy that under stable ion conditions (SbF_5–SO_2ClF, −78 °C) the cation common to 5-norbornen-2-yl and 3-nortricyclyl derivatives apparently has the 3-nortricyclyl structure (**7**).[12] In this work we have confirmed that ionization of **6** leads to a symmetrical intermediate. Acetolysis of optically active **6** gives 5-norbornen-*exo*-2-yl acetate



(−)-**6** **7** **8** (−)-**9**

(**9**) and 3-nortricyclyl acetate (**8**), both of which are racemic.

(+)-5-Norbornen-*exo*-2-ol was prepared as described earlier.[13] Absolute configurations and rotations have been determined for the alcohol and acetate derivative (**8**).[13,14] The (+)-**6** used in the present work was derived from (+)-norbornenol, ~44% optically pure, by a procedure designed to avoid loss of configuration.

The polarimetric rate of acetolysis of (+)-**6** was cleanly first order and k_α was 7.28×10^{-3} min^{-1} at 25 °C (ROBs = 0.04 M; NaOAc = 0.047 M). This is 2.7 times larger than the reported value for the titrimetric rate constant ($k_t = 2.70 \times 10^{-3}$ min^{-1}).[9a] Thus acetolysis is accompanied by ion pair return which results in first-order racemization of the unsolvolyzed ester.

Acetolysis of (+)-**6**, ≥44% optically pure, in buffered acetic acid at 25 °C gave 7% **9** and 93% **8** as expected.[9b] Neither had detectable optical activity. Control experiments showed that (+)-**9** is not racemized under conditions of the acetolysis or isolation. From the average optical purity of (+)-**6** during acetolysis, original purity times k_t/k_α,[15] and the absolute rotation of **9**,[13] it can be shown that 0.5% retention of configuration would result in detectable optical activity. The absolute rotation of **8** is not known. However, that this product is indeed racemic was confirmed with a chiral NMR shift reagent, $Eu(hfbc)_3$.[16] In the presence of this reagent, enantiomers of **8** have nonequivalent NMR spectra, $\Delta\Delta\delta = 0.1$ and 0.08 ppm for the methyl and C-3 proton signal. Thus it seems clear that solvolysis of **6** involves assisted ionization with direct formation of a symmetrical bridged ion (**7**).

Recently Brown and Peters[11] observed that the retarding effect of the double bond for solvolysis of 2-methyl-5-norbornen-2-yl *p*-nitrobenzoate (**10**) in 80% aqueous acetone is the

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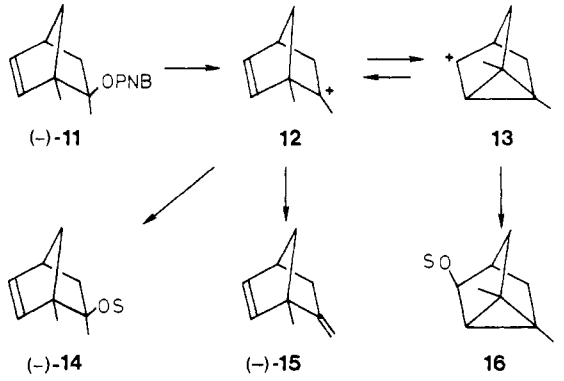
same for the exo and endo isomers. From this it was concluded that π participation provides no significant assistance in tertiary 5-norbornen-*exo*-2-yl systems.

In the present work we have confirmed this conclusion. Solvolysis of optically active 1,2-dimethyl-5-norbornen-*exo*-2-yl *p*-nitrobenzoate (**11**) in 90% aqueous acetone gives active 2-methylene-1-methyl-5-norbornene (**15**) and 1,2-dimethyl-5-norbornen-*exo*-2-ol (**14**-OH). Similarly, methanolysis gives active S_N1 (**14**-OCH_3) and E1 (**15**) products. This shows that



solvolysis involves unassisted ionization to give the classical tertiary ion (**12**). The 1-methyl substituent in **11** has only a small accelerating effect on the rate (~3),[18] and from this we conclude that this substituent does not affect the nature of the ionization. However, it does allow distinguishing between assisted and unassisted ionization on the basis of the symmetry properties of the intermediate.

Table I. Titrimetric (k_t) and Polarimetric (k_α) Rate Constants for Solvolysis of **11**

Temp, °C	$10^4 k_t$, min^{-1}	$10^4 k_\alpha$, min^{-1}	k_α/k_t
	A. 90% Acetone (v/v)		
78.80	0.323 ± 0.002[a]	0.500 ± 0.007[b,c,d]	1.55
100.00	3.45 ± 0.21[a]	5.61 ± 0.24[b,c,d]	1.63
	B. Methanol		
100.00	30.2 ± 0.5[a]	51.4 ± 0.7[b,c,d]	1.70

[a] Substrate concentration 0.004 M. [b] Substrate concentration 0.03 M. [c] Average of constants determined from rotations at four wavelengths. [d] Solvent contained 10% excess 2,6-lutidine.

The preparation of racemic and optically active **11**, **14**-OH, and **14**-OCH_3 and determination of absolute configurations and rotations for these compounds was reported earlier.[17] Titrimetric (k_t) and polarimetric (k_α) rate constants for solvolysis of **11** in 90% (v/v) aqueous acetone and methanol are shown in Table I. All rates are first order and in each solvent $k_\alpha > k_t$. This shows that solvolysis is accompanied by ion pair return that results in racemization of the unsolvolyzed substrate.

A slight excess of 2,6-lutidine was added to the solvent for the polarimetric experiments and product studies to neutralize the acid produced by solvolysis. Under these conditions, initially formed optically active products are stable and the polarimetric rates are first order. It has been shown that in closely related systems small amounts of lutidine has no significant effect on the rate of solvolysis.[1a,2]

The product studies are summarized by eq 1 and 2. These

$$\underset{-88.3°}{(-)\text{-}\mathbf{11}} \xrightarrow[]{90\%\ \text{acetone}} \underset{-1.8°}{30\%\ \mathbf{14}\text{-OH}} + \underset{-153°}{60\%\ \mathbf{15}} + \underset{0.000°}{10\%\ \mathbf{16}\text{-OH}} \quad (1)$$
$$(57\%) \qquad (8.4\%) \qquad (35\%)$$

$$\underset{-88.3°}{(-)\text{-}\mathbf{11}} \xrightarrow[100°]{\text{methanol}} \underset{-6°}{20\%\ \mathbf{14}\text{-}OCH_3} + \underset{-141°}{40\%\ \mathbf{15}} + \underset{0.000°}{40\%\ \mathbf{16}\text{-}OCH_3} \quad (2)$$
$$(54\%) \qquad (7.4\%) \qquad (32\%)$$

equations show the product distributions determined by capillary GC. In each solvent a trace (<1%) of an additional E1 product, 1,2-dimethyl-2,5-norbornadiene, was detected. Optical rotations, $[\alpha]^{25}D$ ($CHCl_3$), are shown beneath each compound and optical purities are shown in parentheses under each rotation. Optical purities were determined from the known absolute rotations.[17] That for **11** has been corrected for racemization that results from ion pair return, i.e., initial optical purity (91%) times k_t/k_α.[15] The substrate concentration was 0.03 M for 90% acetone and 0.02 M for methanolysis.

As shown by the data under eq 1 and 2, solvolysis of optically active **11** gives optically active unrearranged S_N1 (**14**) and E1 (**15**) products and racemic 1,6-dimethyl-3-nortricyclyl derivatives (**16**). In 90% acetone **14**-OH and **15** are formed with 15 and 61% retention of configuration. For methanolysis the substitution (**14**-OCH_3) and elimination (**15**) products are formed with 14 and 59% retention.

These results suggest that unassisted ionization leads to the asymmetric classical ion **12** which isomerizes reversibly to the symmetrical tricyclyl cation **13**. This reversible isomerization accounts for the partial loss of activity in the E1 and S_N1

products derived from **12**. Presumably the racemic 1,6-dimethyl-3-nortricyclyl products (**16**) are derived from **13**.

The rate-retarding effect of the double bond on k_t also suggests unassisted ionization. The **1**-OPNB/**11** ratio in 90% acetone at 100 °C is 23 as compared with a saturated/unsaturated ratio of 11 in 80% acetone at 100 °C for **5a**.[11]

The present results are remarkably similar to those reported for the 1,2-dimethyl-*exo*-2-norbornyl (**1**)[1,19] and 1,2-dimethyl-*exo*-2-benzonorbornenyl systems (**2a**)[2] with regard to retention of configuration in the E1 and S_N1 products. In all cases the E1 product is formed with much more retention of configuration (~60%) than the S_N1 product (~10%). As noted earlier,[1,2] this shows that the E1 and S_N1 products are derived from different intermediates. These results are accommodated by a mechanism proposed earlier[19] in which most, or all, of the E1 product is derived from the initially formed intimate ion pair and the S_N1 product is formed largely, or completely, from a solvent separated ion pair or a dissociated carbonium ion. According to this view, the additional dissociation required for substitution is accompanied by additional racemization.

Experimental Section

A 100-ft SE-30 capillary column was used for analytical GC and a 5 ft × 0.25 in. column packed with 10% FFAP on Chromosorb W 60/80 was used for preparative GC. NMR spectra was determined with a JEOL MH-100 spectrometer. Melting points are not corrected.

Materials. Acetic acid was purified by a published procedure.[20] Analytical grade acetone was dried (Drierite) and fractionated from molecular sieve. Conductivity water was prepared by distillation of laboratory distilled water from potassium permanganate. The 90% aqueous acetone was prepared by mixing nine volumes of acetone and one volume of water at room temperature. Analytical grade methanol was distilled from magnesium. 2,6-Lutidine was distilled first from anhydrous aluminum chloride and then from barium oxide. Analytical grade sodium acetate was dried under high vacuum at 120 °C for 2 days.

(+)-5-Norbornen-*exo*-2-yl *p*-Bromobenzenesulfonate ((+)-6). (+)-5-Norbornen-*exo*-2-yl acetate ((+)-**9**) was prepared by asymmetric hydroboration of norbornadiene as described previously.[13,14] (+)-α-Pinene, $[\alpha]^{20}D$ 46° (neat) (~90% optically pure), was used to prepare the tetraisopinocamphenyldiborane used in the hydroboration. A homogeneous sample of (+)-**9**, $[\alpha]^{25}D$ 27.3° (*c* 0.9, $CHCl_3$), was obtained by preparative GC. NMR (CCl_4) δ 6.20 (d, 1 H), 6.00 (d, 1 H), 4.58 (d of d, 1 H), 2.84 (bs, 2 H), 1.96 (s, 3 H), 1.2–1.8 (m, 4 H). The NMR spectrum corresponds to that reported for *dl*-**9**.[21]

The above (+)-**9** was converted to (+)-5-norbornen-*exo*-2-ol by reduction with lithium aluminum hydride as described earlier.[13] A homogeneous sample obtained by preparative GC had $[\alpha]^{25}D$ 5.3° (*c* 1.3, $CHCl_3$) which corresponds to 44% optical purity.[13] NMR (CCl_4) δ 6.14 (d, 1 H), 5.92 (d, 1 H), 3.8 (bd, 1 H), 3.28 (bs, 1 H, OH), 2.76 (bd, 2 H), 1.6–1.84 (m, 4 H).

A solution of 4.1 g (37.3 mmol) of the above (+)-norbornenol in 23 ml of dry pyridine was cooled to 5 °C, and 11.3 g (44 mmol) of *p*-bromobenzenesulfonyl chloride was added slowly. The cold solution was stirred 5 h and placed in a refrigerator overnight. The reaction mixture was diluted with 250 ml of ice water and extracted with ether. The ether extract was washed with cold 10% hydrochloric acid and then with water. After drying, the ether was removed under reduced pressure. Recrystallization of the residue from hexane gave 9.0 g (73%) of colorless (+)-**6**, mp 56–61 °C, $[\alpha]^{25}D$ 21.9° (*c* 1.3, $CHCl_3$). The rotation increases with recrystallization; thus, the (+)-**6** is at least as optically pure as the norbornenol (44%) from which it was derived. NMR (CCl_4) δ 7.65 (q, 4 H), 6.19 (d of d, 1 H), 5.84 (d of d, 1 H), 4.44 (bt, 1 H), 2.9 (bd, 2 H), 1.4–1.8 (m, 4 H).

Attempts to determine the optical purity (and absolute rotation) of the above (+)-**6** by reconversion to norbornenol were unsuccessful. Reduction with either sodium naphthalene[22] or lithium–ammonia[23] gave mixtures of about 70% *exo*- and 30% *endo*-5-norbornen-2-ol which had negative rotations. The norbornenol mixture from the sodium naphthalene reduction was isolated by preparative GC and had $[\alpha]^{25}D$ −10.6° (*c* 0.56, $CHCl_3$). We were unable to isolated a pure sample of the exo isomer from this mixture.

Kinetic Studies. A. Acetolysis of (+)-5-Norbornen-*exo*-2-yl *p*-Bromobenzenesulfonate ((+)-6). A 0.04 M solution of the above (+)-**6** in acetic acid containing 0.047 M sodium acetate was placed in a 1 dm jacketed polarimeter tube. The tube was thermostated at 25.0 °C and the rotation (α^{25}_{365}) determined at appropriate intervals. The rotation changed from 1.094° at zero time to zero. The reaction was followed to 87% completion. Under these conditions $k_\alpha = 7.27 \pm 0.12 \times 10^{-3}$ min^{-1}; average and average deviation for 29 almost equally spaced points.

B. Solvolysis of 1,2-Dimethyl-5-norbornen-*exo*-2-yl *p*-Nitrobenzoate (11).[17] The titrimetric (k_t) and polarimetric (k_α) rate constants in Table I were obtained by a standard ampule technique. All ampules were degassed and sealed under vacuum. For the polarimetric experiments the solvent contained a 10% excess of 2,6-lutidine. Rotation at four wavelengths, 589, 578, 546, and 436 nm, were determined at appropriate times. Values of k_α in Table **I** are averages of individual determinations for the four wavelengths. As indicated by the average deviations, the four values were similar. Reactions were followed to about 75% completion and good first-order behavior was observed in all cases. For k_t, the reaction was followed by titration of 5-ml aliquots with 0.0197 N aqueous sodium hydroxide.

Acetolysis of (+)-5-Norbornen-*exo*-2-yl *p*-Bromobenzenesulfonate ((+)-6). A solution of 658 mg of the above (+)-**6** in 50 ml of 0.047 M sodium acetate in dry acetic acid was thermostated at 25 °C for 4 days (about 20 half-lives). The resulting solution was diluted with 500 ml of ice water and extracted with pentane. The pentane extract was washed with cold 10% sodium carbonate and then with water. The extract was dried ($MgSO_4$) and concentrated. Analytical GC showed two peaks with a ratio of 7:93. The components were isolated by preparative GC. The minor compound was **9**, α^{25} 0.000° at 589, 578, 546, 436, and 365 nm (*c* 1.14, 1 dm, $CHCl_3$). The (+)-**9** from which the (+)-**6** was derived had α^{25}_{365} 0.921° (*c* 0.86, 1 dm, $CHCl_3$). Complete retention would have led to (+)-**9**, α^{25}_{365} 0.452° (c 1.14, 1 dm, $CHCl_3$). Since rotations can be determined to ±0.002°, 0.5% retention would have been detected. The major component was also optically inactive and identified as 3-nortricyclyl acetate (**8**) from the NMR spectrum, (CCl_4) δ 4.6 (s, 1 H), 2.0 (s, 3 h), 1.25–1.88 (m, 8 H).

A completely independent experiment gave the same results, both **9** and **8** were inactive. That **8** isolated from the product studies is racemic was also indicated from the NMR spectrum in the presence of $Eu(hfbc)_3$.[16] At a shift reagent/substrate ratio of 1.28, ΔΔδ is 0.10 for the methyl signal and 0.08 for the C-3 proton.

In a control experiment a solution of 33 mg of (+)-**9** in 5 ml of 0.047 M sodium acetate in acetic acid, α^{25}_{365} 0.802° (1 dm), was placed in a 25 °C thermostat for 4 days. There was no change in rotations for 589, 578, 546, 436, or 365 nm. Isolation as described above gave only unchanged (+)-**9**. It was also observed that **8** is structurally stable under conditions of solvolysis and isolation.

Solvolysis of (−)-1,2-Dimethyl-5-norbornen-*exo*-2-yl *p*-Nitrobenzoate ((−)-11) in 90% Aqueous Acetone (v/v). In a typical experiment, a solution of 200 mg (0.70 mmol) of (−)-**11**,[17] $[\alpha]^{25}D$ −88.3° (*c* 0.46, $CHCl_3$) (91% optically pure), and 82 mg (0.77 mmol) of 2,6-lutidine in 25 ml of 90% acetone was sealed in a degassed heavy-walled ampule. The solution was heated at 100 °C for 16 days (>10 half-lives). The acetone was carefully removed under reduced pressure and the residue extracted with ether. Analytical GC showed that the dried (Drierite) ether extract contained 60% 2-methylene-1-methyl-5-norbornene (**15**), 10% 1,2-dimethyl-5-norbornen-*exo*-2-ol (**14**-OH), and 30% 1,6-dimethyl-3-nortricyclanol (**16**-OH). Pure **15** was isolated by preparative GC and had $[\alpha]^{25}D$ −153°. The substitution products, **14**-OH and **16**-OH, could not be separated completely by preparative GC. A mixture containing 75% **14**-OH and 25% **16**-OH had $[\alpha]^{25}D$ −1.35° (*c* 0.813, $CHCl_3$). Pure **16**-OH was obtained by chromatography (80:20 ratio of Al_2O_3:$AgNO_3$) with 80:20 ether:pentane as eluent. The pure **16**-OH had no detectable rotation at any of the five wavelengths, 589, 578, 546, 436, and 365 nm (*c* 0.15). The rotation of **14**-OH, corrected for contamination by 25% of racemic **16**-OH, is $[\alpha]^{25}D$ 1.8°. Optically purities of the products and the average optical purity of the (−)-**11** (91% × k_t/k_α = 57%) are shown under eq 1.

Control experiments showed that **14**-OH and **15** are optically and structurally stable under the conditions of solvolysis and isolation.

Methanolysis of (−)-1,2-Dimethyl-5-norbornen-*exo*-2-yl *p*-Nitrobenzoate ((−)-11). A solution of 560 mg (1.95 mmol) of (−)-**11**, $[\alpha]^{25}D$ −88.3°, and 229.4 mg (2.14 mmol) of 2,6-lutidine in 120 ml of methanol was sealed in a heavy-walled ampule and heated at 100

°C for 12 half-lives. The products were isolated as described in the preceding section. Analytical GC showed that the product distribution was 40% **15** and 60% of a mixture of **14**-OCH_3 and **16**-OCH_3. This mixture could not be resolved by analytical GC and the composition of a sample isolated by preparative GC was determined by NMR as a 1:2 mixture of **14**-OCH_3 and **16**-OCH_3. Thus, methanolysis of **11** gives 40% **15**, 20% **14**-OCH_3, and 40% **16**-OCH_3. The optical rotation of pure **15**, isolated by preparative GC, was $[\alpha]^{25}D$ −141°. The mixture of 33% **14**-OCH_3 and 66% **16**-OCH_3 had $[\alpha]^{25}D$ −2.10° (*c* 0.428, $CHCl_3$). Pure **16**-OCH_3 was separated from this mixture by column chromatography (80:20 mixture of Al_2O_3 and $AgNO_3$ with pentane as eluent) and showed no activity at 589, 578, 546, 436, or 365 nm, (*c* 0.413 $CHCl_3$): NMR (CCl_4) δ 3.40 (s, 1 H, C-3 methine proton), 3.16 (s, 3 H, methoxy methyl), 1.9 (s, 1 H, bridgehead), 0.8–1.76 (m, 4 H), 1.2 (s, 3 H), 1.1 (s, 3 H), 0.48 (s, 1 H, cyclopropyl). The rotation of **14**-OCH_3, corrected for contamination with 66% racemic **16**-OCH_3 is $[\alpha]^{25}D$ −6.0° (*c* 0.14, $CHCl_3$). Optical purities of the products and the average optical purity of the (−)-**11** during methanolysis (91% × k_t/k'_α) are shown under eq 2.

Authentic samples of optically active **15** and **14**-OCH_3[17] were shown to be optically stable under conditions of the solvolysis and isolation of the products.

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Positive Cooperativity in Micelle-Catalyzed Reactions

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Abstract: The rate constants of micelle-catalyzed reactions when plotted vs. detergent concentration give sigmoid shaped curves. This behavior is analogous to positive cooperativity in enzymatic reactions, a sigmoid shaped dependence of velocity on substrate concentration. A kinetic model analogous to the Hill model, which describes enzymatic reactions, accommodates published data on the rate constants of micellar reactions as a function of detergent concentration. According to this model, plots of log $[(k_{obsd} - k_0)/(k_m - k_{obsd})]$ vs. detergent concentration are linear, and have slopes equal to the empirical constant *n*; the term log $[D]_{50}$ is also easily ascertained from these plots as that detergent concentration at which the rate constant of micellar catalysis is one-half of its maximal value. Published data on the dependence of rate constants on detergent concentration were evaluated according to this model. Values of *n* ranged from approximately 1 to 6 with the vast majority of reactions having values of *n* below 3. For a given reaction, the nature of the detergent appeared to have an effect on both log $[D]_{50}$ and *n*. Log $[D]_{50}$ paralleled the log of the critical micelle concentration for a variety of detergents catalyzing the hydrolysis of methyl orthobenzoate, but the two were not related in a simple manner. When a single detergent was employed, and variations in the structure of the substrate were made, effects were seen on both log $[D]_{50}$ and *n*. However, major structural variations in the substrates were required; alterations of electronic inductive effects were not always sufficient. The inhibition and activation of micelle-catalyzed reactions by substances which are neither substrate nor detergent could be described in analogy with the terminology of enzymology. V-type inhibitors and activators are substances which affect the maximum attainable velocity; K-type inhibitors and activators are substances which affect the value of log $[D]_{50}$. Examples of V-type inhibitors, V-type activators, and K-type inhibitors of micelle-catalyzed reactions were found. In addition to having their effects on the maximum attainable velocity, k_m, and log $[D]_{50}$, these substances also affected the value of *n*. Micellar catalysis is treated here in analogy with the Hill model for enzymatic cooperativity for the sake of simplicity. Micellar catalysis may also be described in terms of the Monod–Wyman–Changeux and Koshland–Nemethy–Filmer models, which require different conformational forms of free and substrate bound catalyst.

In attempting to elucidate the mechanisms by which enzymes effect catalysis, chemists have expended a great deal of effort in studying mechanisms of simpler, model chemical reactions.[1] Among these models have been reactions catalyzed within micelles.[2,3] Although the analogy between micelle-catalyzed reactions and enzyme-catalyzed reactions is far from perfect, there are important similarities.[3] The structures of both micelles and enzymes are similar in that they have hydrophobic cores with polar groups on their surfaces. The structures of micelles are disrupted by common protein denaturing agents such as urea and guanidinium salts. Both catalytic micelles and enzymes bind substrates in a noncovalent